```
=> fil reg
FILE 'REGISTRY' ENTERED AT 13:06:05 ON 08 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:     7 MAY 2004  HIGHEST RN 680859-76-1
DICTIONARY FILE UPDATES:    7 MAY 2004  HIGHEST RN 680859-76-1

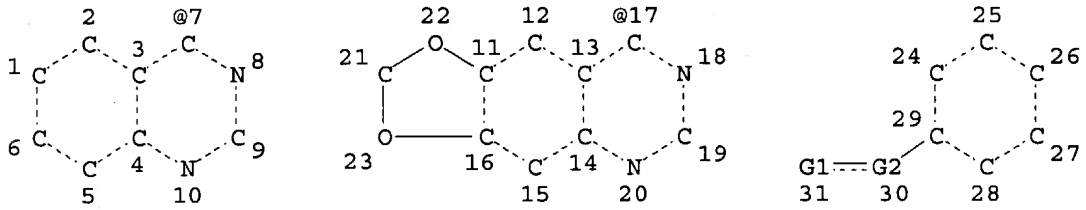
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d sta que l31
L24                 STR
```




```
VAR G1=7/17
VAR G2=N/S/O/C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   1  11
NUMBER OF NODES IS  31

STEREO ATTRIBUTES: NONE
L26        13458 SEA FILE=REGISTRY SSS FUL L24
L27              STR
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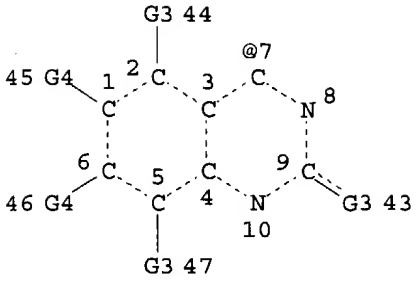
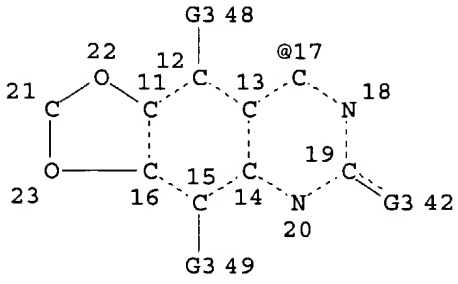
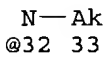
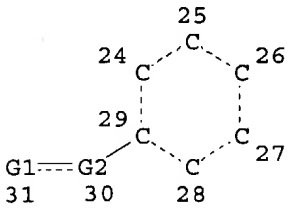
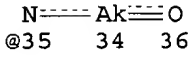
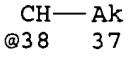


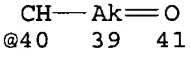


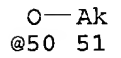


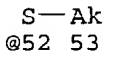


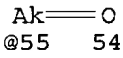








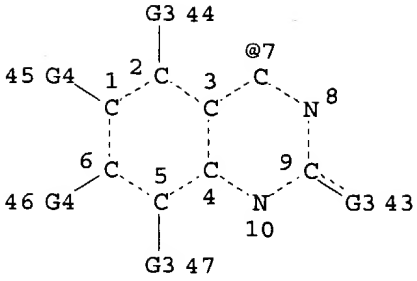


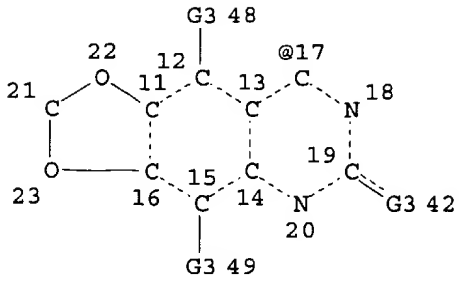


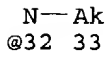
VAR G1=7/17
VAR G2=NH/32/35/S/O/38/40
VAR G3=H/OH/S/N/NO2/AK/50/52/X
VAR G4=H/AK/50/X/55
NODE ATTRIBUTES:
CONNECT IS M1 RC AT 21
CONNECT IS M1 RC AT 24
CONNECT IS M1 RC AT 25
CONNECT IS M1 RC AT 26
CONNECT IS M1 RC AT 27
CONNECT IS M1 RC AT 28
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

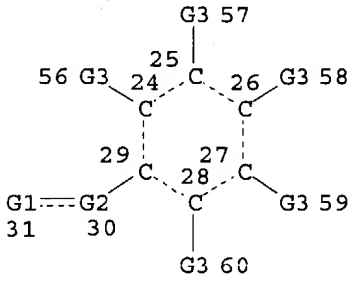
GRAPH ATTRIBUTES:
RSPEC 1 11
NUMBER OF NODES IS 55

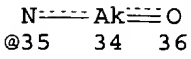
STEREO ATTRIBUTES: NONE
L29 2935 SEA FILE=REGISTRY SUB=L26 CSS FUL L27
L30 STR

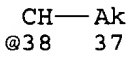


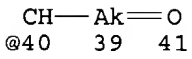


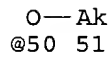


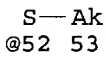


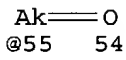












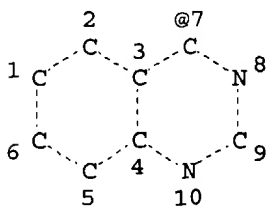
VAR G1=7/17
VAR G2=NH/32/35/S/O/38/40
VAR G3=H/OH/S/N/NO2/AK/50/52/X
VAR G4=H/AK/50/X/55
NODE ATTRIBUTES:
CONNECT IS M1 RC AT 21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

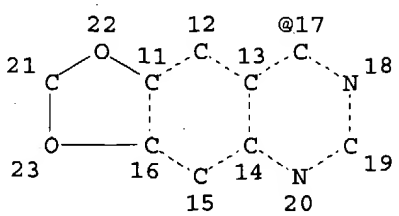
GRAPH ATTRIBUTES:
RSPEC 1 11 24
NUMBER OF NODES IS 60

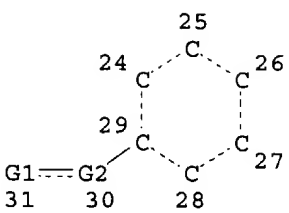
STEREO ATTRIBUTES: NONE
L31 997 SEA FILE=REGISTRY SUB=L29 CSS FUL L30

100.0% PROCESSED 2782 ITERATIONS 997 ANSWERS
SEARCH TIME: 00.00.01

=> d sta que l33
L24 STR



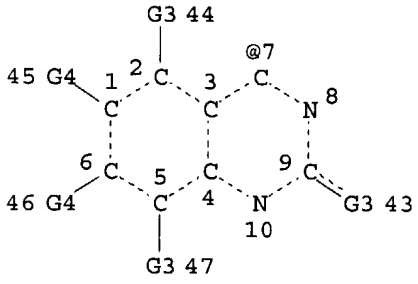


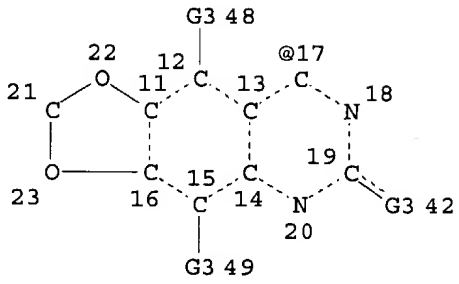


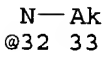
VAR G1=7/17
VAR G2=N/S/O/C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

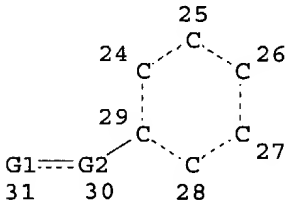
GRAPH ATTRIBUTES:
RSPEC 1 11
NUMBER OF NODES IS 31

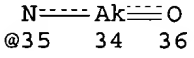
STEREO ATTRIBUTES: NONE
L26 13458 SEA FILE=REGISTRY SSS FUL L24
L27 STR

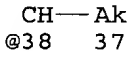


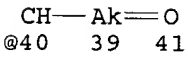


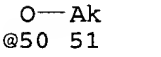


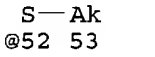


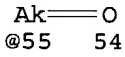








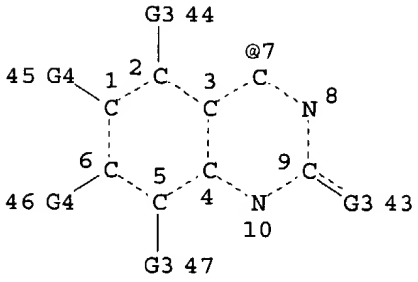


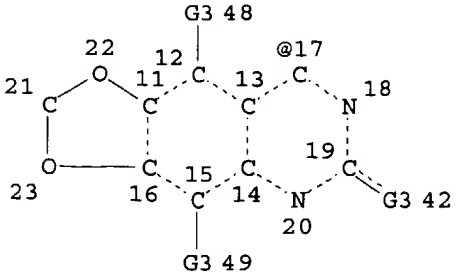


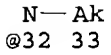
VAR G1=7/17
VAR G2=NH/32/35/S/O/38/40
VAR G3=H/OH/S/N/NO2/AK/50/52/X
VAR G4=H/AK/50/X/55
NODE ATTRIBUTES:
CONNECT IS M1 RC AT 21
CONNECT IS M1 RC AT 24
CONNECT IS M1 RC AT 25
CONNECT IS M1 RC AT 26
CONNECT IS M1 RC AT 27
CONNECT IS M1 RC AT 28
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

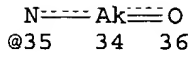
GRAPH ATTRIBUTES:
RSPEC 1 11
NUMBER OF NODES IS 55

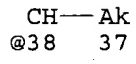
STEREO ATTRIBUTES: NONE
L29 2935 SEA FILE=REGISTRY SUB=L26 CSS FUL L27
L32 STR

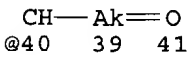


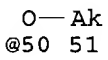


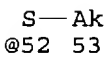


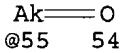


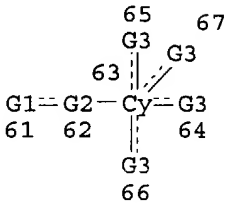












VAR G1=7/17
VAR G2=NH/32/35/S/O/38/40
VAR G3=H/OH/S/N/NO2/AK/50/52/X
VAR G4=H/AK/50/X/55
NODE ATTRIBUTES:
CONNECT IS M1 RC AT 21
DEFAULT MLEVEL IS ATOM
GGCAT IS PCY AT 63
DEFAULT ECLEVEL IS LIMITED

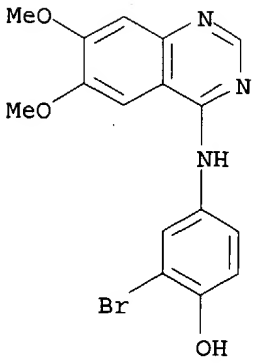
GRAPH ATTRIBUTES:
RSPEC 1 11
NUMBER OF NODES IS 54

STEREO ATTRIBUTES: NONE
L33 116 SEA FILE=REGISTRY SUB=L29 CSS FUL L32

100.0% PROCESSED 2935 ITERATIONS 116 ANSWERS
SEARCH TIME: 00.00.01

=> d ide can tot l7

L7 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN **211555-04-3** REGISTRY
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN WHI-P 154
FS 3D CONCORD
MF C16 H14 Br N3 O3
CI COM
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, IMSDRUGNEWS, IMSRESEARCH, PHAR, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

26 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
26 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:246485

REFERENCE 2: 139:358316

REFERENCE 3: 139:173786

REFERENCE 4: 139:144001

REFERENCE 5: 138:248178

REFERENCE 6: 138:71823

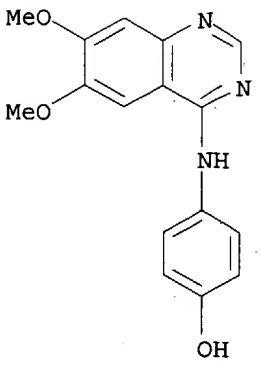
REFERENCE 7: 138:20416

REFERENCE 8: 135:41029

REFERENCE 9: 134:363426

REFERENCE 10: 133:271682

L7 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN **202475-60-3** REGISTRY
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4-(4'-Hydroxyphenyl)amino-6,7-dimethoxyquinazoline
CN Janex 1
CN WHI-P 131
FS 3D CONCORD
MF C16 H15 N3 O3
CI COM
SR CA
LC STN Files: ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, EMBASE, IMSDRUGNEWS, IMSRESEARCH, MEDLINE, PHAR, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

33 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
35 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:174738

REFERENCE 2: 140:23256

REFERENCE 3: 139:301736

REFERENCE 4: 139:173786

REFERENCE 5: 139:159929

REFERENCE 6: 139:144001

REFERENCE 7: 137:320073

REFERENCE 8: 136:272618

REFERENCE 9: 135:221035

REFERENCE 10: 135:132432

=> d his

(FILE 'REGISTRY' ENTERED AT 12:38:55 ON 08 MAY 2004)
DEL HIS

FILE 'HCAPLUS' ENTERED AT 12:39:03 ON 08 MAY 2004
L1 1 S US20030144178/PN OR WO99-US14923/AP,PRN
E UCKUM F/AU
L2 459 S E4-E11
E HUGHES/AP,CS
E HUGHES/PA,CS
L3 20026 S E3,E4
E HUGHES INS/PA,CS
L4 37 S E5-E16
L5 8669 S (HUGHES(L)INSTITUTE?)/PA,CS
SEL RN L1

FILE 'REGISTRY' ENTERED AT 12:41:02 ON 08 MAY 2004
L6 6 S E1-E6

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L7            2 S L6 AND 3/NR
                SEL RN
L8           22 S E7-E8/CRN
L9           19 S L8 NOT (MXS/CI OR OC4/ES)
L10          11 S L9 NOT (COMPD OR WITH)
L11           8 S L9 NOT L10
L12           3 S L8 NOT L9

     FILE 'HCAPLUS' ENTERED AT 12:43:22 ON 08 MAY 2004
L13          42 S L7
L14           6 S L10
L15          41 S WHI()(P154 OR P131 OR P()(154 OR 131))
L16           9 S 4 4 HYDROXYPHENYL AMINO 6 7 DIMETHOXYQUINAZOLINE
L17           3 S 4 3 BROMO 4 HYDROXYPHENYL AMINO 6 7 DIMETHOXYQUINAZOLINE
L18           5 S 4 3 BROMO 4 HYDROXYLPHENYL AMINO 6 7 DIMETHOXYQUINAZOLINE
L19           3 S 4 4 HYDROXYLPHENYL AMINO 6 7 DIMETHOXYQUINAZOLINE
L20          58 S L13-L19
L21          39 S L2 AND L20
L22          39 S L3-L5 AND L20
L23          39 S L21,L22

     FILE 'REGISTRY' ENTERED AT 12:46:58 ON 08 MAY 2004
L24             STR
L25          50 S L24
L26       13458 S L24 FUL
                SAV TEMP L26 HOPE345/A
L27             STR L24
L28          50 S L27 CSS SAM SUB=L26
L29        2935 S L27 CSS FUL SUB=L26
                SAV TEMP L29 HOPE345A/A
L30             STR L27
L31         997 S L30 CSS FUL SUB=L29
                SAV L31 HOPE345B/A
L32             STR L30
L33         116 S L32 CSS FUL SUB=L29
                SAV L33 HOPE345C/A
L34        1113 S L31,L33
L35        1100 S L34 NOT L7,L10

     FILE 'HCAPLUS' ENTERED AT 12:58:54 ON 08 MAY 2004
L36         357 S L35
L37          19 S L2 AND L36
L38          18 S L3-L5 AND L36
L39          41 S L23,L37,L38
L40           8 S L39 AND (PY<=1998 OR PRY<=1998 OR AY<=1998)
L41         392 S L20,L36
L42         192 S L41 AND (PY<=1998 OR PRY<=1998 OR AY<=1998)
L43           5 S L42 AND JAK#

     FILE 'REGISTRY' ENTERED AT 13:01:33 ON 08 MAY 2004
L44           1 S 157482-36-5
                E KINASE (PHOSPHORYLATING), JAK/CN
L45           4 S E4,E6,E25,E47
L46          66 S E4-E69 NOT L45

     FILE 'HCAPLUS' ENTERED AT 13:03:20 ON 08 MAY 2004
L47        2230 S L44,L45,L46
L48         323 S (JAK3 OR JAK 3)()(JANUS KINASE OR KINASE OR PROTEIN KINASE OR
L49         709 S JANUS KINASE 3 OR JAK KINASE OR PROTEIN KINASE JAK3 OR LEUKOC
L50           5 S L42 AND L47-L49
L51          10 S L40,L43,L50
L52           3 S L42 AND JAK 3
L53          10 S L51,L52
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L54 3 S L42 AND (CJUN OR C JUN)
L55 11 S L53,L54

FILE 'REGISTRY' ENTERED AT 13:06:05 ON 08 MAY 2004

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 13:06:43 ON 08 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 8 May 2004 VOL 140 ISS 20
FILE LAST UPDATED: 7 May 2004 (20040507/ED)

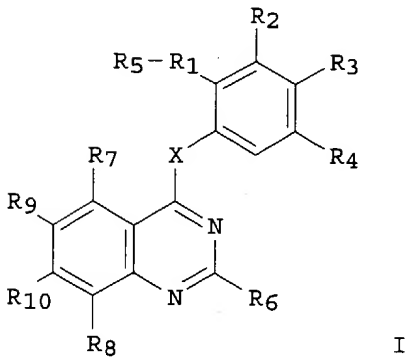
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l55 all hitstr tot

L55 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:610073 HCAPLUS
DN 139:144001
ED Entered STN: 08 Aug 2003
TI Preparation of quinazoline derivatives as **JAK-3** **kinase** inhibitors and their therapeutic uses
IN Fatih, M. Uckun
PA USA
SO U.S. Pat. Appl. Publ., 103 pp., Cont.-in-part of U.S. Pat. Appl. 2001 44,442.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-525
ICS A61K031-517
NCL 514251000; 514266100; 514266300; 514266400
CC 1-12 (Pharmacology)
Section cross-reference(s): 28, 63
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 2003149045	A1	20030807	US 2002-211045	20020802	
	US 6313129	B1	20011106	US 1999-378093	19990820	<--
	US 2001044442	A1	20011122	US 2001-812098	20010319	<--
	US 6495556	B2	20021217			
	US 2002042513	A1	20020411	US 2001-858824	20010516	<--
	US 6469013	B2	20021022			
PRAI	US 1999-378093	A1	19990820			
	US 2001-812098	A2	20010319			
	US 2001-309557P	P	20010802			
	US 2001-309558P	P	20010802			
	US 1998-97359P	P	19980821	<--		

US 1998-97365P P 19980821 <--
US 2000-688756 A3 20001016
OS MARPAT 139:144001
GI



I

AB The invention provides novel **JAK-3** inhibitors that are useful for treating leukemia and lymphoma. The compds. I [X is NH, R11N, S, O, CH2, or R11CH; R11is H, (C1-C4)alkyl, or (C1-C4)alkanoyl; R1-R8 are each independently H, OH, mercapto, NH2, NO, (C1-C4)alkyl, (C1-C4)alkoxy, (C1-C4)alkylthio, or halo; wherein two adjacent groups of R1-R5 together with the Ph ring may optionally form a fused ring that can be substituted; and R9 and R10 are each independently H, (C1-C4)alkyl, (C1-C4)alkoxy, halo, or (C1-C4)alkanoyl; or R9 and R10 together are methylenedioxy] are also useful to treat or prevent skin cancer, as well as sunburn and UVB-induced skin inflammation. In addition, the compds. of the present invention prevent the immunosuppressive effects of UVB radiation, and are useful to treat or prevent autoimmune diseases, inflammation, and transplant rejection. The invention also provides pharmaceutical compns. comprising compds. of the invention, as well as therapeutic methods for their use. Specifically claimed in this CIP patent is a pharmaceutical composition containing quinazoline derivs. in combination with methotrexate to treat GVHD.

ST quinazoline deriv prepn antitumor antiinflammatory immunosuppressant

IT Drug delivery systems
(GVHD prevention with compns. containing quinazoline derivs. in combination with an immunosuppressant; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Immunosuppressants
(GVHD prevention with quinazoline derivs. in combination with an immunosuppressant; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Dermatitis
(UV B-induced prevention; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Enzyme functional sites
(active, conformation of the quinazoline derivs. docked to the catalytic site of **JAK3**; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Leukemia
(acute lymphocytic, treatment; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Transplant and Transplantation

(allotransplant, bone marrow, inhibition of transplant complications; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Bone marrow
(allotransplant, inhibition of transplant complications; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Diabetes mellitus
(autoimmune induced diabetes; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Transplant and Transplantation
(bone marrow, inhibition of transplant complications; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Conformation
(conformation of the quinazoline derivs. docked to the catalytic site of **JAK3**; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Radiation
(damage, prevention of skin cancer from UVB radiation; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Skin, disease
(edema, prevention of skin edema from UVB radiation exposure; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Structure-activity relationship
(enzyme-inhibiting; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Transplant and Transplantation
(graft-vs.-host reaction, inhibition of transplant complications; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Neutrophil
(infiltration, prevention of neutrophil infiltration in skin after UVB radiation exposure; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Transplant and Transplantation
Transplant rejection
(inhibition of transplant complications; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Cell migration
(neutrophil infiltration, prevention of neutrophil infiltration in skin after UVB radiation exposure; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Transplant and Transplantation
(pancreatic islet, inhibition of transplant complications; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Anti-inflammatory agents
Antidiabetic agents
Antitumor agents
Human
Molecular modeling
Pharmacophores
(preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Skin, neoplasm
UV B radiation
(prevention of skin cancer from UVB radiation; preparation of quinazoline

derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Inflammation
(prevention; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Sunburn
(protection against; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Bone marrow
Pancreatic islet of Langerhans
(transplant, inhibition of transplant complications; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT Autoimmune disease
Leukemia
Lymphoma
(treatment; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT **572895-68-2 572895-69-3 572895-70-6 572895-71-7**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GVHD prevention with compns. containing quinazoline derivs. in combination with an immunosuppressant; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT 59-05-2, Methotrexate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GVHD prevention with quinazoline derivs. in combination with an immunosuppressant; preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT **157482-36-5, JAK-3 kinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT **21561-09-1P**, WHI-P258 **153436-54-5P**, WHI-P79 **202475-60-3P**, **WHI-P131 211555-04-3P**, **WHI-P154 211555-05-4P**, WHI-P97 **211555-06-5P**, WHI-P111 **211555-07-6P**, WHI-P132 **211555-08-7P**, WHI-P180 **211555-09-8P**, WHI-P197 **247080-98-4P**, WHI-P 112 **251376-04-2P**, WHI-P292
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT 64-18-6, Formic acid, reactions 4998-07-6, 4,5-Dimethoxy-2-nitrobenzoic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT 4959-60-8P, 4,5-Dimethoxy-2-nitrobenzamide 5004-88-6P, 4,5-Dimethoxy-2-aminobenzamide 13790-39-1P 13794-72-4P, 6,7-Dimethoxyquinazoline-4(3H)-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)

IT **572895-68-2 572895-69-3 572895-70-6 572895-71-7**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GVHD prevention with compns. containing quinazoline derivs. in combination

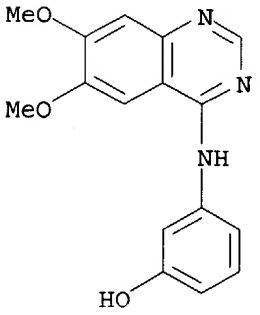
with an immunosuppressant; preparation of quinazoline derivs. as **JAK -3 kinase** inhibitors and their therapeutic uses)

RN 572895-68-2 HCAPLUS

CN L-Glutamic acid, N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]-, mixt. with 3-[(6,7-dimethoxy-4-quinazolinyl)amino]phenol (9CI) (CA INDEX NAME)

CM 1

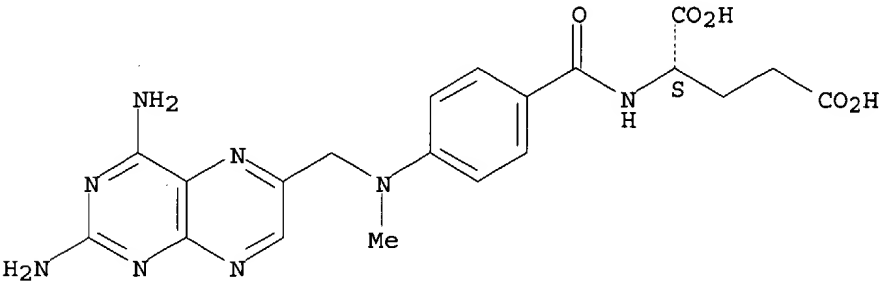
CRN 211555-08-7
CMF C16 H15 N3 O3



CM 2

CRN 59-05-2
CMF C20 H22 N8 O5

Absolute stereochemistry.

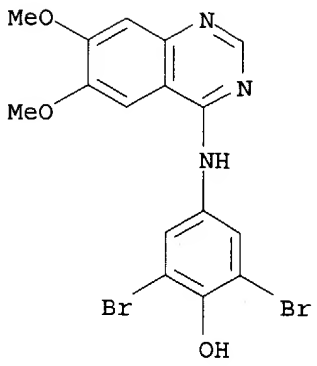


RN 572895-69-3 HCAPLUS

CN L-Glutamic acid, N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]-, mixt. with 2,6-dibromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenol (9CI) (CA INDEX NAME)

CM 1

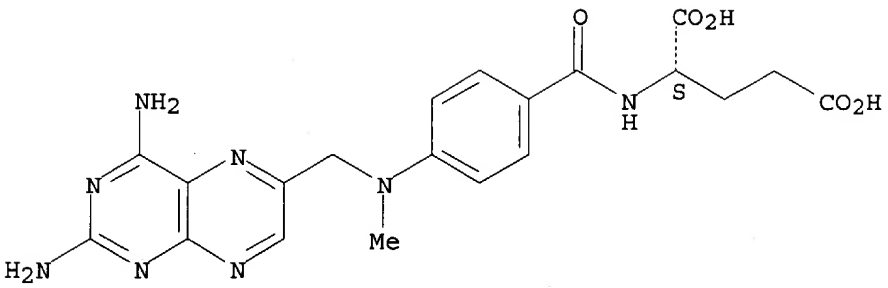
CRN 211555-05-4
CMF C16 H13 Br2 N3 O3



CM 2

CRN 59-05-2
CMF C20 H22 N8 O5

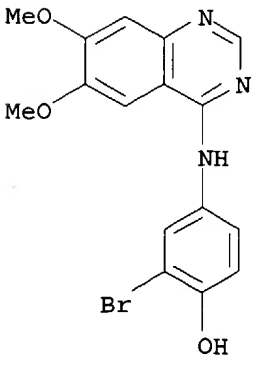
Absolute stereochemistry.



RN 572895-70-6 HCAPLUS
CN L-Glutamic acid, N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]-, mixt. with 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenol (9CI) (CA INDEX NAME)

CM 1

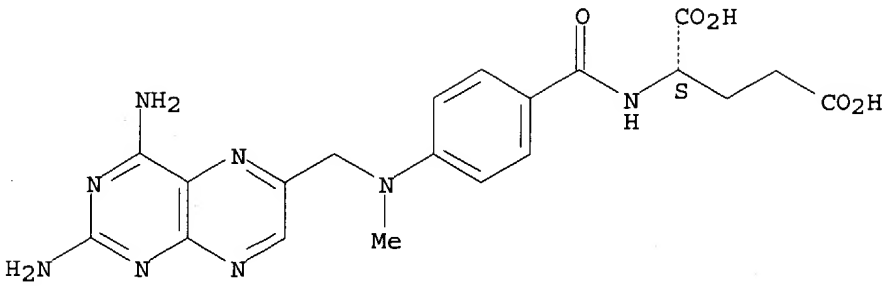
CRN 211555-04-3
CMF C16 H14 Br N3 O3



CM 2

CRN 59-05-2
CMF C20 H22 N8 O5

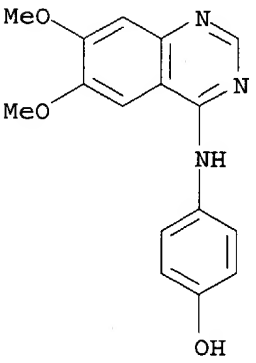
Absolute stereochemistry.



RN 572895-71-7 HCAPLUS
CN L-Glutamic acid, N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]-, mixt. with 4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenol (9CI) (CA INDEX NAME)

CM 1

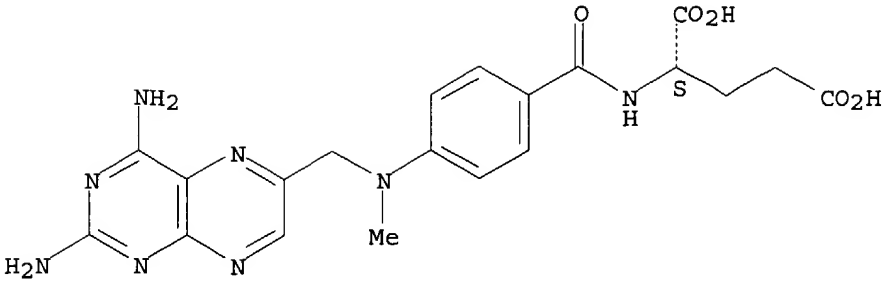
CRN 202475-60-3
CMF C16 H15 N3 O3



CM 2

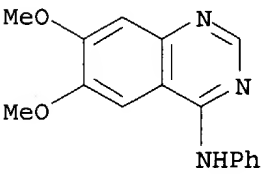
CRN 59-05-2
CMF C20 H22 N8 O5

Absolute stereochemistry.

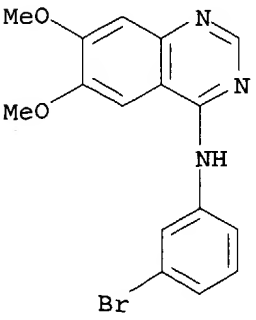


IT **157482-36-5, JAK-3 kinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **21561-09-1P**, WHI-P258 **153436-54-5P**, WHI-P79
202475-60-3P, **WHI-P131** **211555-04-3P**,
WHI-P154 **211555-05-4P**, WHI-P97
211555-06-5P, WHI-P111 **211555-07-6P**, WHI-P132
211555-08-7P, WHI-P180 **211555-09-8P**, WHI-P197
247080-98-4P, WHI-P 112 **251376-04-2P**, WHI-P292
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazoline derivs. as **JAK-3 kinase** inhibitors and their therapeutic uses)
RN 21561-09-1 HCAPLUS
CN 4-Quinazolinamine, 6,7-dimethoxy-N-phenyl- (9CI) (CA INDEX NAME)



RN 153436-54-5 HCAPLUS
CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



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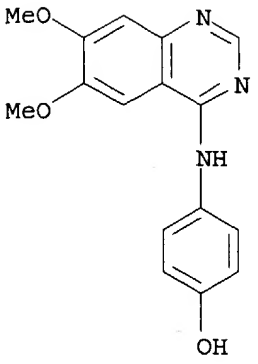
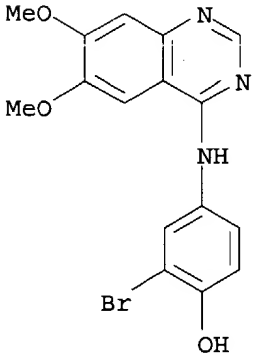
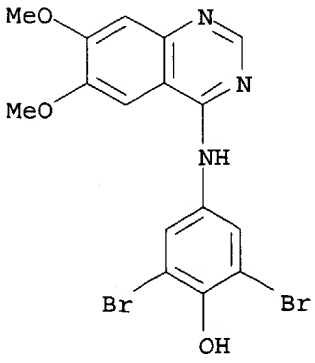


RN 211555-04-3 HCAPLUS
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 211555-05-4 HCAPLUS
CN Phenol, 2,6-dibromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



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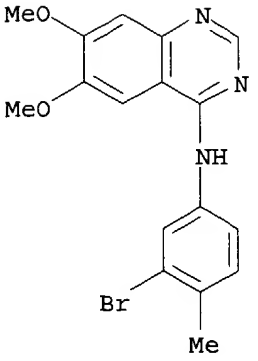

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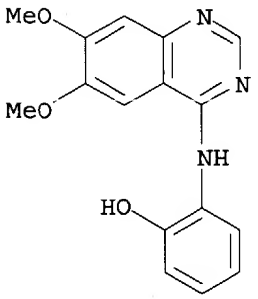

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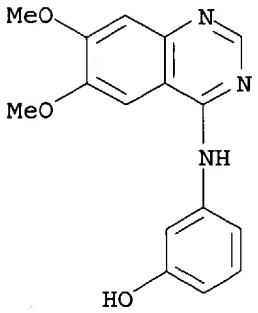

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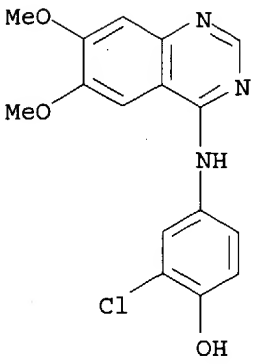

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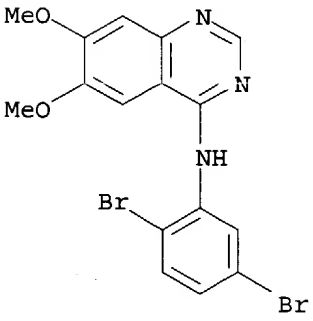

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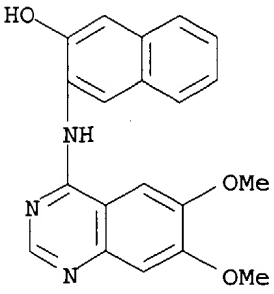

L55 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:144864 HCAPLUS
DN 132:189690
ED Entered STN: 03 Mar 2000
TI Therapeutic uses of quinazoline derivatives as **JAK**-3 **kinase** inhibitors
IN Navara, Christopher S.; Mahajan, Sandeep; **Uckun, Fatih M.**
PA **Hughes Institute, USA**
SO PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DT Patent

LA English
IC C07D239-94; A61P035-02; A61P037-06; A61K031-505
CC 1-12 (Pharmacology)
Section cross-reference(s): 28, 63
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2000010981	A1	20000302	WO 1999-US19043	19990820	<--
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
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	AU 9956827	A1	20000314	AU 1999-56827	19990820	<--
	EP 1105378	A1	20010613	EP 1999-943800	19990820	<--
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	JP 2002523403	T2	20020730	JP 2000-566255	19990820	<--
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	US 2002042513	A1	20020411	US 2001-858824	20010516	<--
	US 6469013	B2	20021022			
PRAI	US 1998-97359P	P	19980821	<--		
	US 1998-97365P	P	19980821	<--		
	US 1999-378093	A3	19990820			
	WO 1999-US19043	W	19990820			
	US 2000-688756	A3	20001016			

OS MARPAT 132:189690
AB The invention provides novel **JAK-3 kinase** inhibitors that are useful for treating leukemia and lymphoma. The compds. are also useful to treat or prevent skin cancer, as well as sunburn and UVB-induced skin inflammation. In addition, the compds. of the present invention prevent the immunosuppressive effects of UVB radiation, and are useful to treat or prevent autoimmune diseases, inflammation, and transplant rejection. The invention also provides pharmaceutical compns. comprising compds. of the invention, as well as therapeutic methods for their use. For example, treatments with 50 mg/kg or 75 mg/kg of a quinazoline derivative **WHI-P131** (preparation given) were as effective as cyclosporin A treatment in prolongation of islet allograft survival in mice.
ST quinazoline deriv antitumor antiinflammatory immunosuppressant; **JAK3 kinase** inhibitor quinazoline deriv
IT T cell (lymphocyte)
(activation, inhibition of; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
IT Transplant and Transplantation
Transplant and Transplantation
(bone marrow; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
IT Skin, disease
(edema, UVB-induced; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
IT Structure-activity relationship
(enzyme-inhibiting; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
IT Skin
(epithelium, damage of; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
IT Transplant and Transplantation

(graft-vs.-host reaction; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
IT UV B radiation
(inflammation induced by; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
IT Skin, neoplasm
Skin, neoplasm
(inhibitors; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
IT Antitumor agents
(leukemia; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
IT Antitumor agents
(lymphoma; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
IT Transplant and Transplantation
Transplant and Transplantation
(pancreatic islet; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
IT Blood vessel
(permeability; therapeutic uses of quinazoline derivs. as **JAK -3 kinase** inhibitors)
IT Antitumor agents
Antitumor agents
(skin; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
IT Anti-inflammatory agents
Antidiabetic agents
Apoptosis
Autoimmune disease
Immunosuppressants
Sunburn
Transplant rejection
(therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
IT Bone marrow
Bone marrow
Pancreatic islet of Langerhans
Pancreatic islet of Langerhans
(transplant; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
IT **211555-06-5P**, WHI-P 111
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(WHI-P 111; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
IT **211555-07-6P**, WHI-P 132
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(WHI-P 132; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
IT **211555-09-8P**, WHI-P 197
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(WHI-P 197; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
IT **21561-09-1P**, WHI-P 258
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(WHI-P 258; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)

IT **251376-04-2P**, WHI-P 292
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(WHI-P 292; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)

IT **153436-54-5P**, WHI-P 79
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(WHI-P 79; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)

IT **211555-05-4P**, WHI-P 97
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(WHI-P 97; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)

IT 363-24-6, Prostaglandin E2
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibition of release of; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)

IT **211555-04-3P**, **WHI-P154** **211555-08-7P**, WHI-P180 **247080-98-4P**, WHI-P 112
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)

IT **202475-60-3P**, **WHI-P131**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)

IT **157482-36-5**, **Jak3 kinase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)

IT 123-30-8, p-Hydroxyaniline 4998-07-6, 4,5-Dimethoxy-2-nitrobenzoic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)

IT 4959-60-8P, 4,5-Dimethoxy-2-nitrobenzamide 5004-88-6P 13790-39-1P 13794-72-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Bridges, A; Journal of Medicinal Chemistry 1996, V39, P267 HCAPLUS
(2) Budesinsky, Z; Collect Czech Chem Commun 1972, V37(8), P2779 HCAPLUS
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(19) Sugen Inc; WO 9640648 A 1996 HCAPLUS
(20) Univ Johns Hopkins Med; WO 9618639 A 1996 HCAPLUS
(21) Wellcome Found; WO 9609294 A 1996 HCAPLUS

IT **211555-06-5P**, WHI-P 111
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(WHI-P 111; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
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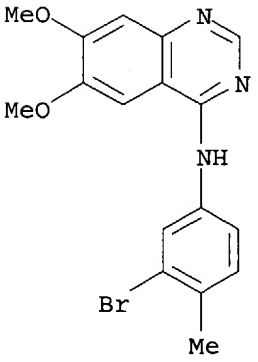

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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(WHI-P 132; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
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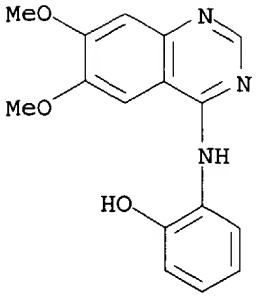

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(WHI-P 197; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
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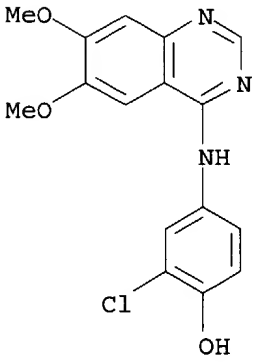

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(WHI-P 258; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
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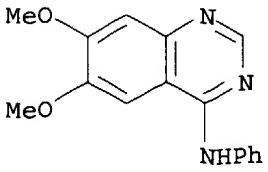

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(WHI-P 292; therapeutic uses of quinazoline derivs. as **JAK-**

3 kinase inhibitors)
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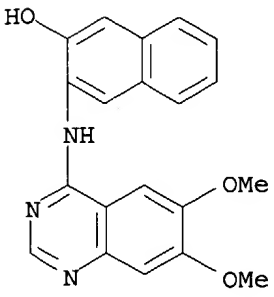

IT **153436-54-5P**, WHI-P 79
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(WHI-P 79; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
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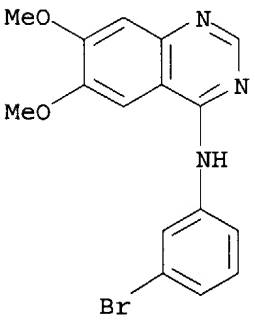

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(WHI-P 97; therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
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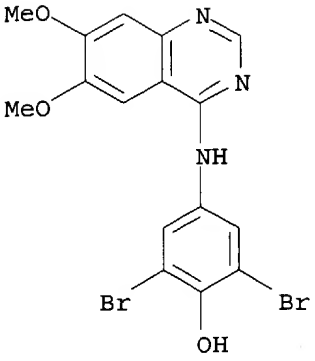

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(therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
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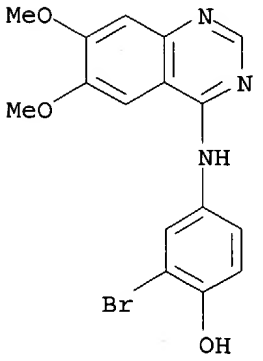

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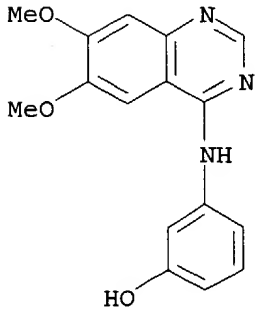

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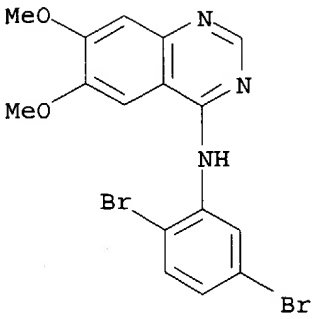

IT **202475-60-3P, WHI-P131**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
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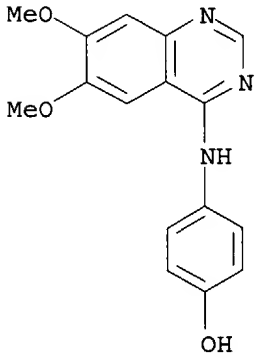


IT **157482-36-5, Jak3 kinase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(therapeutic uses of quinazoline derivs. as **JAK-3 kinase** inhibitors)
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L55 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:98531 HCAPLUS
DN 132:137404
ED Entered STN: 11 Feb 2000
TI Preparation of lipid-lowering quinazoline derivatives
IN **Uckun, Fatih M.**; Trieu, Vuong N.; Liu, Xing-Ping
PA Wayne **Hughes Institute**, USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D239-74
ICS A61K031-517

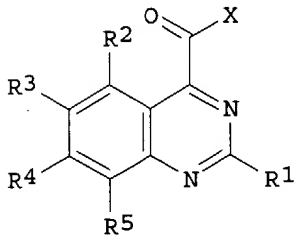
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2000006554	A1	20000210	WO 1999-US15841	19990713	<--
	W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	US 6172071	B1	20010109	US 1998-126940	19980730	<--
	CA 2338825	AA	20000210	CA 1999-2338825	19990713	<--
	AU 9949913	A1	20000221	AU 1999-49913	19990713	<--
	AU 750653	B2	20020725			
	EP 1100787	A1	20010523	EP 1999-933976	19990713	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
	JP 2002521475	T2	20020716	JP 2000-562357	19990713	<--
	US 2001008894	A1	20010719	US 2001-756483	20010108	<--
	US 6355645	B2	20020312			
	NO 2001000525	A	20010130	NO 2001-525	20010130	<--
	US 2001051629	A1	20011213	US 2001-892047	20010626	<--
PRAI	US 1998-126940	A	19980730	<--		
	WO 1999-US15841	W	19990713			
	US 2001-754483	A1	20010104			

OS MARPAT 132:137404

GI



I

AB A novel carbonyl-substituted quinazolines [I; X = a straight or branched chain or cyclic alkyl, or an aryl; R1-R5 = H, OH, NH2, etc.], preferably 4-(3'-bromobenzoyl)-6,7-dimethoxyquinazoline [WHI-P164], useful for lowering blood cholesterol, including reducing total cholesterol and LDL-cholesterol levels, were prepared Biol. data for compds. I were given.

ST lipid lowering quinazoline prepn; anticholesteremic quinazoline prepn; LDL cholesterol quinazoline prepn

IT Lipoproteins
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(low-d.; preparation of lipid-lowering quinazoline derivs.)

IT Anticholesteremic agents
(preparation of lipid-lowering quinazoline derivs.)

IT **202475-60-3P 211555-04-3P 211555-05-4P**
211555-06-5P 211555-07-6P 211555-09-8P
256532-03-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of lipid-lowering quinazoline derivs.)

IT 3132-99-8, 3-Bromobenzaldehyde 4998-07-6, 4,5-Dimethoxy-2-nitrobenzoic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of lipid-lowering quinazoline derivs.)

IT 4959-60-8P, 4,5-Dimethoxy-2-nitrobenzamide 13790-39-1P 13794-72-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of lipid-lowering quinazoline derivs.)

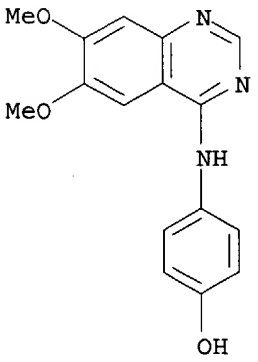
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

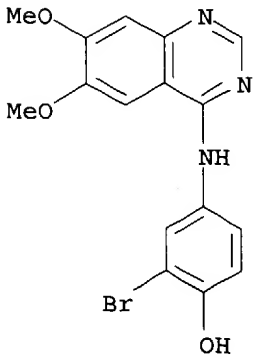
(1) Rhone-Poulenc; WO 9515758 A 1995 HCAPLUS
(2) Suzuki, Y; CHEMICAL AND PHARMACEUTICAL BULLETIN 1998, V46(2) HCAPLUS
(3) Taylor, E; GEN PROCEDURE FOR THE SYNTHESIS OF EPOXYALKYLATED AND ACYLATED HETEROCYCLES 1974, 26, P337 HCAPLUS
(4) Taylor, E; HETEROCYCLES 1973, V1(1-2), P59 HCAPLUS

IT **202475-60-3P 211555-04-3P 211555-05-4P**
211555-06-5P 211555-07-6P 211555-09-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of lipid-lowering quinazoline derivs.)

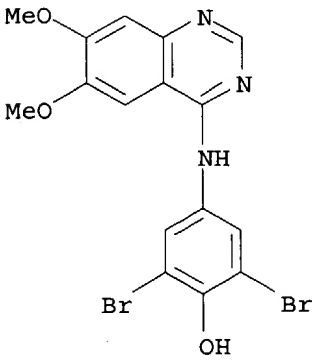
RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



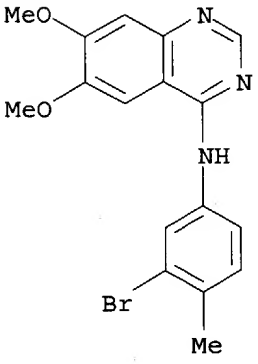
RN 211555-04-3 HCAPLUS
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



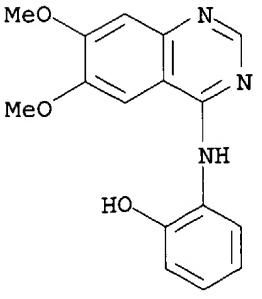
RN 211555-05-4 HCAPLUS
CN Phenol, 2,6-dibromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



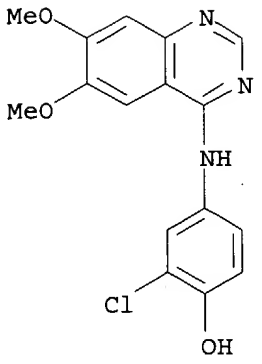
RN 211555-06-5 HCAPLUS
CN 4-Quinazolinamine, N-(3-bromo-4-methylphenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



RN 211555-07-6 HCAPLUS
CN Phenol, 2-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 211555-09-8 HCAPLUS
CN Phenol, 2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L55 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:15019 HCAPLUS
DN 132:64268
ED Entered STN: 07 Jan 2000
TI Preparation of 4-anilinoquinazolines and analogs as **JAK3** inhibitors
IN **Uckun, Fatih M.**
PA **Hughes Institute, USA**
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-517
ICS C07D243-34
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2000000202	A1	20000106	WO 1999-US14923	19990630	<--
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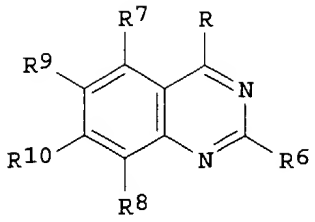
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	CA 2337999	AA	20000106	CA 1999-2337999	19990630	<--
	AU 9948515	A1	20000117	AU 1999-48515	19990630	<--
	EP 1091739	A1	20010418	EP 1999-932145	19990630	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	JP 2004504259	T2	20040212	JP 2000-556787	19990630	<--
	US 2003144178	A1	20030731	US 2001-838821	20010419	<--
PRAI	US 1998-91150P	P	19980630	<--		
	US 1999-345815	A3	19990630			
	WO 1999-US14923	W	19990630			

OS MARPAT 132:64268
GI



I

AB Title compds. [I; R = ZR1; R1 = (un)substituted Ph; R6-R8 = H, halo, alkyl, alkoxy, etc.; R9,R10 = H, halo, alkyl, alkoxy,alkanoyl; R9R10 = OCH2O; Z = CHR11, O, S, NR11; R11 = H, alkyl, alkanoyl] were prepared Thus, I (R6-R8 = H, R9 = R10 = OMe)(II; R = Cl) was aminated by 4-(HO)C6H4NH2 to give II [R = NHC6H4(OH)-4]. Data for biol. activity of I were given.

ST anilinoquinazoline prepn **JAK3** inhibitor; **cjun** expression inhibitor anilinoquinazoline prepn

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**c-jun**, mediated disorders; treatment; preparation of 4-anilinoquinazolines and analogs as **JAK3** inhibitors)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(oncogene, mediated disorders; treatment; preparation of 4-anilinoquinazolines and analogs as **JAK3** inhibitors)

IT Antitumor agents
(preparation of 4-anilinoquinazolines and analogs as **JAK3** inhibitors)

IT **157482-36-5**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mediated disorders; treatment; preparation of 4-anilinoquinazolines and analogs as **JAK3** inhibitors)

IT **202475-60-3P 211555-04-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-anilinoquinazolines and analogs as **JAK3** inhibitors)

IT 123-30-8, 4-Hydroxyaniline 13790-39-1, 4-Chloro-6,7-dimethoxyquinazoline 16750-67-7, 4-Amino-2-bromophenol
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 4-anilinoquinazolines and analogs as **JAK3** inhibitors)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Goodman, P; J Biol Chem 1998, V273, P17742 HCAPLUS
(2) Leonard, W; WO 9703358 A 1997 HCAPLUS
(3) Narla, R; Clinical Cancer Research V4(6), P1405 HCAPLUS
(4) St Jude Childrens Res Hospital; WO 9503701 A 1995 HCAPLUS

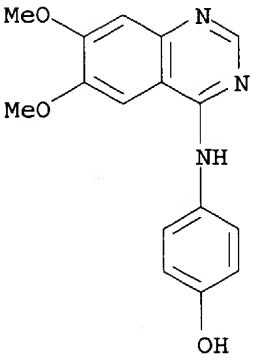
IT **157482-36-5**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mediated disorders; treatment; preparation of 4-anilinoquinazolines and analogs as **JAK3** inhibitors)

RN 157482-36-5 HCAPLUS

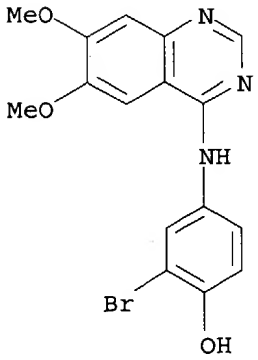
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **202475-60-3P 211555-04-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-anilinoquinazolines and analogs as **JAK3** inhibitors)
RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 211555-04-3 HCAPLUS
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L55 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:764027 HCAPLUS
DN 132:9009
ED Entered STN: 03 Dec 1999
TI Quinazolines and conjugates thereof for treating brain tumors
IN **Uckun, Fatih M.**; Narla, Rama K.; Liu, Xing-Ping
PA Wayne **Hughes Institute**, USA
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D239-94
ICS C07D239-88; C07D239-74; A61K031-505
CC 1-6 (Pharmacology)
Section cross-reference(s): 2, 28, 63
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 9961428	A1	19991202	WO 1999-US11767	19990528 <--
	W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2333392	AA	19991202	CA 1999-2333392	19990528 <--
	AU 9943173	A1	19991213	AU 1999-43173	19990528 <--
	EP 1082311	A1	20010314	EP 1999-953336	19990528 <--
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	JP 2002516823	T2	20020611	JP 2000-550834	19990528 <--
	US 6316454	B1	20011113	US 1999-361088	19990726 <--
	NO 2000005864	A	20010129	NO 2000-5864	20001120 <--
	US 2002161226	A1	20021031	US 2001-903294	20010711
	US 6552027	B2	20030422		
PRAI	US 1998-87479	A	19980529 <--		
	WO 1999-US11767	W	19990528		
	US 1999-361088	A1	19990726		

OS MARPAT 132:9009

AB Substituted quinazoline compds. and conjugates useful for inhibiting the growth of brain tumor cells and for inhibiting adhesion and migration of brain tumor cells are provided. The compds. include **4-(3'-bromo-4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline** and this compound covalently bound to e.g. EGF.

ST quinazoline deriv brain cancer treatment; EGF quinazoline conjugate brain cancer treatment; adhesion brain cancer cell quinazoline deriv; migration brain cancer cell quinazoline deriv

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibodies to, conjugates; quinazoline derivs., preparation, conjugates, and use for treating brain tumors)

IT Structure-activity relationship
(antitumor; quinazoline derivs., preparation, conjugates, and use for treating brain tumors)

IT Antitumor agents
Antitumor agents
(brain; quinazoline derivs., preparation, conjugates, and use for treating brain tumors)

IT Antibodies
Cytokines
Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates; quinazoline derivs., preparation, conjugates, and use for treating brain tumors)

IT Neuroglia
(glioblastoma, cell adhesion; quinazoline derivs., preparation, conjugates, and use for treating brain tumors)

IT Neuroglia
Neuroglia
(glioblastoma, inhibitors; quinazoline derivs., preparation, conjugates, and use for treating brain tumors)

IT Antitumor agents
(glioblastoma; quinazoline derivs., preparation, conjugates, and use for treating brain tumors)

IT Brain, neoplasm
Brain, neoplasm
(inhibitors; quinazoline derivs., preparation, conjugates, and use for treating brain tumors)
IT Brain, neoplasm
(medulloblastoma, cell adhesion; quinazoline derivs., preparation, conjugates, and use for treating brain tumors)
IT Antitumor agents
(metastasis; quinazoline derivs., preparation, conjugates, and use for treating brain tumors)
IT Actins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(polymerization; quinazoline derivs., preparation, conjugates, and use for treating
brain tumors)
IT Apoptosis
Cell adhesion
Cell migration
Drug delivery systems
Drug targeting
(quinazoline derivs., preparation, conjugates, and use for treating brain tumors)
IT Epidermal growth factor receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(quinazoline derivs., preparation, conjugates, and use for treating brain tumors)
IT Biological transport
(uptake; quinazoline derivs., preparation, conjugates, and use for treating brain tumors)
IT **211555-04-3DP**, **WHI-P154**, EGF conjugates
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(quinazoline derivs., preparation, conjugates, and use for treating brain tumors)
IT 62229-50-9, Epidermal growth factor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(quinazoline derivs., preparation, conjugates, and use for treating brain tumors)
IT **21561-09-1P**, WHI-P 258 **153436-54-5P**, WHI-P 79
202475-60-3P, **WHI-P131** **211555-04-3P**,
WHI-P154 **211555-05-4P**, WHI-P 97
211555-06-5P, WHI-P 111 **211555-07-6P**, WHI-P 132
211555-08-7P, WHI-P180 **211555-09-8P**, WHI-P 197
251376-04-2P, WHI-P 292
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(quinazoline derivs., preparation, conjugates, and use for treating brain tumors)
IT 62229-50-9D, Epidermal growth factor, quinazoline derivative conjugates
202475-60-3D, **WHI-P131**, EGF conjugates
251347-48-5 **251347-49-6** **251347-50-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quinazoline derivs., preparation, conjugates, and use for treating brain tumors)
IT 62-53-3, Benzenamine, reactions 95-55-6, 2-Hydroxyaniline 123-30-8,

4-Hydroxyaniline 591-19-5, 3-Bromoaniline 591-27-5, 3-Hydroxyaniline 609-21-2, 3,5-Dibromo-4-hydroxyaniline 2834-92-6 3964-52-1, 3-Chloro-4-hydroxyaniline 7745-91-7, 3-Bromo-4-methylaniline 13790-39-1, 4-Chloro-6,7-dimethoxyquinazoline 16750-67-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; quinazoline derivs., preparation, conjugates, and use for treating brain tumors)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

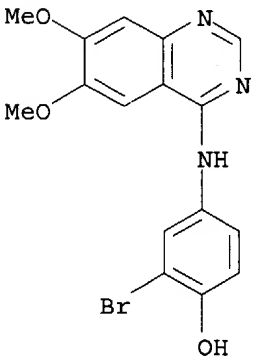
RE

(1) Narla, R; Clinical Cancer Research 1998, V4(6), P1405 HCAPLUS
(2) Rhone-Poulenc; WO 9515758 A 1995 HCAPLUS
(3) Zeneca; EP 0566226 A 1993 HCAPLUS
(4) Zeneca; WO 9615118 A 1996 HCAPLUS
(5) Zeneca; WO 9730035 A 1997 HCAPLUS
(6) Zeneca; WO 9732856 A 1997 HCAPLUS

IT **211555-04-3DP**, **WHI-P154**, EGF conjugates
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(quinazoline derivs., preparation, conjugates, and use for treating brain tumors)

RN 211555-04-3 HCAPLUS

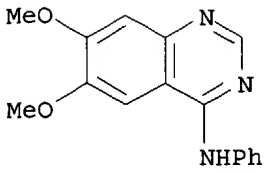
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **21561-09-1P**, WHI-P 258 **153436-54-5P**, WHI-P 79
202475-60-3P, **WHI-P131** **211555-04-3P**,
WHI-P154 **211555-05-4P**, WHI-P 97
211555-06-5P, WHI-P 111 **211555-07-6P**, WHI-P 132
211555-08-7P, WHI-P180 **211555-09-8P**, WHI-P 197
251376-04-2P, WHI-P 292
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(quinazoline derivs., preparation, conjugates, and use for treating brain tumors)

RN 21561-09-1 HCAPLUS

CN 4-Quinazolinamine, 6,7-dimethoxy-N-phenyl- (9CI) (CA INDEX NAME)



RN 153436-54-5 HCAPLUS
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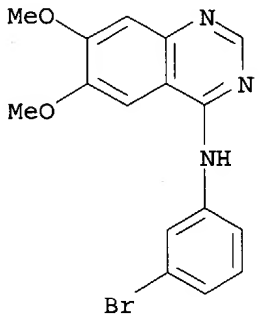

RN 202475-60-3 HCAPLUS
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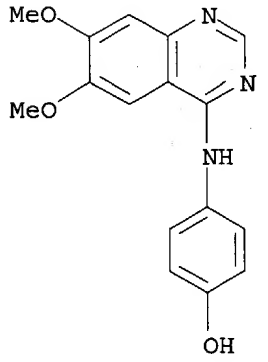

RN 211555-04-3 HCAPLUS
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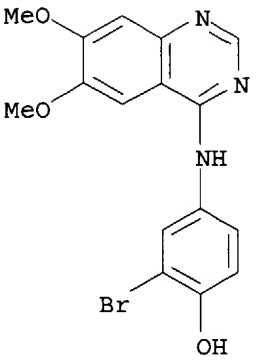

RN 211555-05-4 HCAPLUS
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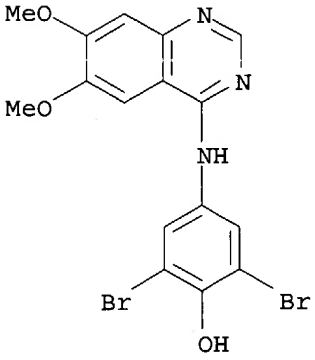

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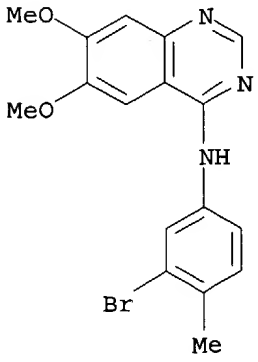

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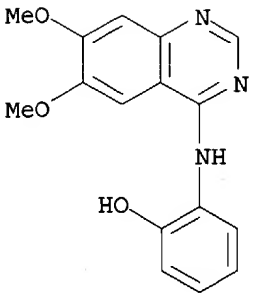

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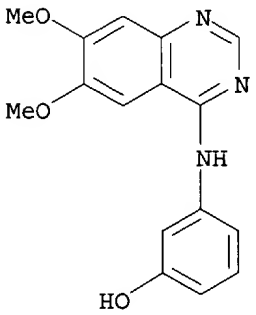

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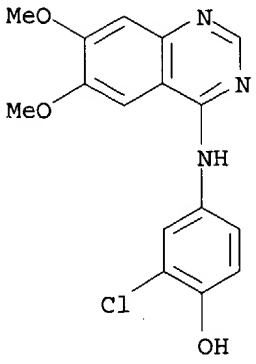
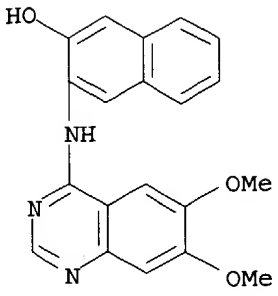
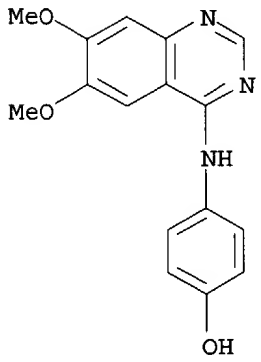


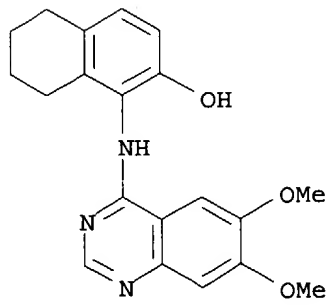
RN 251376-04-2 HCAPLUS
CN 2-Naphthalenol, 3-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



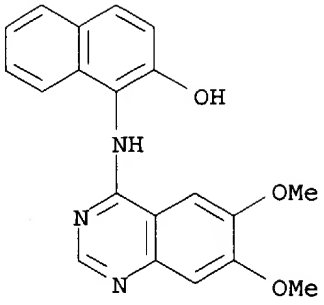
IT **202475-60-3D**, **WHI-P131**, EGF conjugates
251347-48-5 251347-49-6 251347-50-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quinazoline derivs., preparation, conjugates, and use for treating brain tumors)
RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



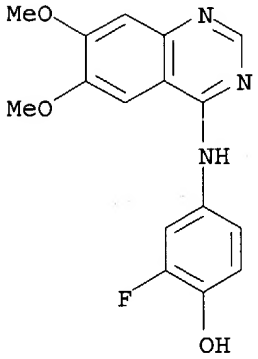
RN 251347-48-5 HCAPLUS
CN 2-Naphthalenol, 1-[(6,7-dimethoxy-4-quinazolinyl)amino]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



RN 251347-49-6 HCAPLUS
CN 2-Naphthalenol, 1-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 251347-50-9 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]-2-fluoro- (9CI) (CA INDEX NAME)



L55 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:659226 HCAPLUS
DN 131:281600
ED Entered STN: 15 Oct 1999
TI Methods and compositions for reducing UV-induced inhibition of collagen synthesis in human skin
IN Fisher, Gary J.; Voorhees, John J.
PA The Regents of the University of Michigan, USA
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-20
ICS A61K031-12; A61K031-235; A61K031-35; A61K031-17
CC 1-12 (Pharmacology)
Section cross-reference(s): 62, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9951220	A1	19991014	WO 1999-US7267	19990402 <--
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2326507	AA	19991014	CA 1999-2326507	19990402 <--

AU 9936374 A1 19991025 AU 1999-36374 19990402 <--
AU 740569 B2 20011108
BR 9909899 A 20001226 BR 1999-9899 19990402 <--
EP 1067920 A1 20010117 EP 1999-918456 19990402 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2002510621 T2 20020409 JP 2000-541991 19990402 <--
US 6683069 B1 20040127 US 1999-285860 19990402 <--
PRAI US 1998-80437P P 19980402 <--
WO 1999-US7267 W 19990402

AB Exposure of human skin to UV radiation from the sun not only induces the production of enzymes (matrix metalloproteinases) that degrade collagen, but also inhibits the synthesis of new collagen by inhibiting the synthesis of procollagen. This UV-induced inhibition of the synthesis of collagen can be prevented by the topical application of a retinoid or **c-JUN** inhibitor to the skin prior to its exposure to UV radiation. It was shown that retinoids such as retinoic acid protect human skin in vivo against the UV-induced inhibition of collagen synthesis.

ST UV inhibition collagen synthesis retinoid

IT Ionophores
(antagonists; retinoids for reducing UV-induced inhibition of collagen synthesis in human skin)

IT G proteins (guanine nucleotide-binding proteins)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; retinoids for reducing UV-induced inhibition of collagen synthesis in human skin)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**c-jun**; retinoids for reducing UV-induced inhibition of collagen synthesis in human skin)

IT Collagens, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(procollagens; retinoids for reducing UV-induced inhibition of collagen synthesis in human skin)

IT Antioxidants
Skin
Sunscreens
UV radiation
(retinoids for reducing UV-induced inhibition of collagen synthesis in human skin)

IT Collagens, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(retinoids for reducing UV-induced inhibition of collagen synthesis in human skin)

IT Retinoids
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(retinoids for reducing UV-induced inhibition of collagen synthesis in human skin)

IT Drug delivery systems
(topical; retinoids for reducing UV-induced inhibition of collagen synthesis in human skin)

IT 62229-50-9, Egf
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; retinoids for reducing UV-induced inhibition of collagen synthesis in human skin)

IT 100324-81-0, Lisofylline 152121-30-7, SB202190 167869-21-8, PD98059
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**c-JUN** inhibitor; retinoids for reducing UV-induced inhibition of collagen synthesis in human skin)

IT 37277-79-5, Geranyltransferase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitor; retinoids for reducing UV-induced inhibition of collagen synthesis in human skin)

IT 145-63-1, Suramin 446-72-0, Genistein 2826-26-8, Tyrphostin 1 118409-57-7, Tyrphostin 23 118409-59-9, Tyrphostin 46 118409-60-2, Tyrphostin 47 125697-92-9, Lavendustin A 126433-07-6, Tyrphostin 51 133550-35-3, AG-494 **153436-54-5**, PD 153035
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ionophore or G-protein or EGF receptor antagonist; retinoids for reducing UV-induced inhibition of collagen synthesis in human skin)

IT 100827-28-9D, Erbstatin, analogs
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ionophore or G-protein or EGF receptor antagonists; retinoids for reducing UV-induced inhibition of collagen synthesis in human skin)

IT 68-26-8, Retinol 302-79-4, Retinoic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(retinoids for reducing UV-induced inhibition of collagen synthesis in human skin)

IT 5466-77-3, 2-Ethylhexyl p-methoxycinnamate 70356-09-1, 4-tert-Butyl-4'-methoxydibenzoylmethane
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sunscreen; retinoids for reducing UV-induced inhibition of collagen synthesis in human skin)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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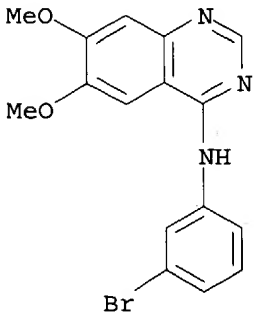
(2) Kligman; US 5051449 A 1991 HCAPLUS
(3) Murray; US 4810489 A 1989 HCAPLUS
(4) Wei; US 5824702 A 1998 HCAPLUS

IT **153436-54-5**, PD 153035
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ionophore or G-protein or EGF receptor antagonist; retinoids for reducing UV-induced inhibition of collagen synthesis in human skin)

RN 153436-54-5 HCAPLUS

CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



L55 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:698779 HCAPLUS

DN 130:104886

ED Entered STN: 04 Nov 1998

TI Inhibition of human glioblastoma cell adhesion and invasion by **4-(4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P131)** and **4-(3'-bromo-4'-hydroxylphenyl)-amino-6,7-**

dimethoxyquinazoline (WHI-P154)

AU Narla, Rama Krishna; Liu, Xing-Ping; Klis, Daniel; **Uckun, Fatih M.**
CS Drug Discovery Program, Department of Experimental Oncology, Wayne **Hughes Institute**, St. Paul, MN, 55113, USA

SO Clinical Cancer Research (**1998**), 4(10), 2463-2471
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
CC 1-6 (Pharmacology)

AB Glioblastoma multiforme is a highly invasive primary brain tumor with a disappointingly high local recurrence rate and mortality despite intensive multimodality treatment programs. Therefore, new agents that are capable of inhibiting the infiltration of normal brain parenchyma by glioblastoma cells are urgently needed. Here, we show that the novel quinazoline derivs. **4-(4'hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P131)** and **4-(3'-bromo-4'hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P154)** are potent inhibitors of glioblastoma cell adhesion and migration. Specifically, both compds. inhibited at micromolar concns.: (a) integrin-mediated glioblastoma cell adhesion to the extracellular matrix proteins laminin, type IV collagen, and fibronectin; (b) integrin-independent epidermal growth factor-induced adhesion of glioblastoma cells to poly-L-lysine-coated tissue culture plates; (c) fetal bovine serum-induced polymerization of actin and actin stress fiber formation as well epidermal growth factor-stimulated formation of focal adhesion plaques in serum-starved glioblastoma cells; and most importantly, (d) glioblastoma cell migration in in vitro assays of tumor cell invasiveness using tumor cell spheroids and/or Matrigel-coated Boyden chambers. Further preclin. development of **WHI-P131** and **WHI-P154** may provide the basis for the design of more effective adjuvant chemotherapy programs for glioblastoma multiforme.

ST glioblastoma cell adhesion migration dimethoxyquinazoline WHIP131 WHIP154

IT Neuroglia
(glioblastoma multiforme; inhibition of human glioblastoma cell adhesion and invasion by the dimethoxyquinazolines **WHI-P131** and **WHI-P154**)

IT Neuroglia
(glioblastoma, inhibitors; inhibition of human glioblastoma cell adhesion and invasion by the dimethoxyquinazolines **WHI-P131** and **WHI-P154**)

IT Antitumor agents
(glioblastoma; inhibition of human glioblastoma cell adhesion and invasion by the dimethoxyquinazolines **WHI-P131** and **WHI-P154**)

IT Cell adhesion
Cell migration
(inhibition of human glioblastoma cell adhesion and invasion by the dimethoxyquinazolines **WHI-P131** and **WHI-P154**)

IT Actins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibition of serum-induced actin polymerization and actin stress fiber formation in human glioblastoma cells by the dimethoxyquinazolines **WHI-P131** and **WHI-P154**)

IT Extracellular matrix
(integrin-mediated glioblastoma cell adhesion to extracellular matrix proteins; inhibition of human glioblastoma cell adhesion and invasion by the dimethoxyquinazolines **WHI-P131** and

WHI-P154)
IT Integrins
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(integrin-mediated glioblastoma cell adhesion to extracellular matrix proteins; inhibition of human glioblastoma cell adhesion and invasion by the dimethoxyquinazolines **WHI-P131** and **WHI-P154**)
IT Fibronectins
Laminins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(integrin-mediated glioblastoma cell adhesion to extracellular matrix proteins; inhibition of human glioblastoma cell adhesion and invasion by the dimethoxyquinazolines **WHI-P131** and **WHI-P154**)
IT Organelle
(stress fiber; inhibition of serum-induced actin polymerization and actin stress fiber formation in human glioblastoma cells by the dimethoxyquinazolines **WHI-P131** and **WHI-P154**)
IT Collagens, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(type IV, integrin-mediated glioblastoma cell adhesion to extracellular matrix proteins; inhibition of human glioblastoma cell adhesion and invasion by the dimethoxyquinazolines **WHI-P131** and **WHI-P154**)
IT 62229-50-9, Epidermal growth factor
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(EGF-induced adhesion and formation of focal adhesion plaques; inhibition of human glioblastoma cell adhesion and invasion by the dimethoxyquinazolines **WHI-P131** and **WHI-P154**)
IT **202475-60-3, WHI-P 131**
211555-04-3, WHI-P 154
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of human glioblastoma cell adhesion and invasion by the dimethoxyquinazolines **WHI-P131** and **WHI-P154**)
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
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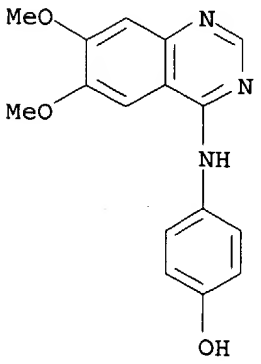
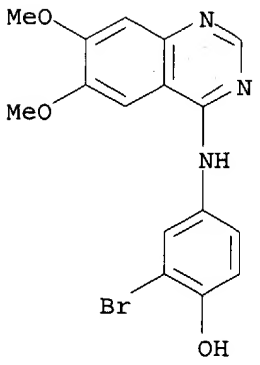
IT **202475-60-3**, **WHI-P 131**
211555-04-3, **WHI-P 154**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of human glioblastoma cell adhesion and invasion by the dimethoxyquinazolines **WHI-P131** and **WHI-P154**)

RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 211555-04-3 HCAPLUS
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L55 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:529827 HCAPLUS
ED Entered STN: 21 Aug 1998
TI **4-(3'-bromo-4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P154)**: A novel quinazoline derivative with potent cytotoxic activity against human glioblastoma cells
AU Narla, R. K.; Liu, X.; Myers, D. E.; Venkatachalam, T.; **Uckun, F. M.**
CS Department Experimental Oncology, Wayne **Hughes Institute**, St. Paul, MN, 55113, USA
SO Book of Abstracts, 216th ACS National Meeting, Boston, August 23-27 (**1998**), MEDI-342 Publisher: American Chemical Society, Washington, D. C.
CODEN: 66KYA2
DT Conference; Meeting Abstract
LA English
AB The novel quinazoline **WHI-P154** exhibited significant cytotoxicity against two glioblastoma cell lines causing apoptotic cell death at micromolar concns. In vitro anti-glioblastoma activity of **WHI-P154** was amplified>200-fold and rendered selective by conjugation to EGF. In vitro treatment with EGF-P154 resulted in killing of glioblastoma cells at nanomolar concns. In vivo administration of EGF-P154 resulted in delayed tumor progression and improved tumor-free survival in a SCID mouse glioblastoma xenograft model. Thus, targeting **WHI-P154** to the EGF-R may be useful in the treatment of glioblastoma.

L55 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:492839 HCAPLUS
DN 129:213579
ED Entered STN: 07 Aug 1998
TI Role of tyrosine kinases in induction of the **c-jun** proto-oncogene in irradiated B-lineage lymphoid cells
AU Goodman, Patricia A.; Niehoff, Lisa B.; **Uckun, Fatih M.**
CS Department of Molecular Genetics, Wayne **Hughes Institute**, St. Paul, MN, 55113, USA
SO Journal of Biological Chemistry (**1998**), 273(28), 17742-17748
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 8-7 (Radiation Biochemistry)
Section cross-reference(s): 28
AB Exposure of B-lineage lymphoid cells to ionizing radiation induces an

elevation of **c-jun** proto-oncogene mRNA levels. This signal is abrogated by protein-tyrosine kinase (PTK) inhibitors, indicating that activation of an as yet unidentified PTK is mandatory for radiation-induced **c-jun** expression. Here, we provide exptl. evidence that the cytoplasmic tyrosine kinases BTK, SYK, and LYN are not required for this signal. Lymphoma B-cells rendered deficient for LYN, SYK, or both by targeted gene disruption showed increased **c-jun** expression levels after radiation exposure, but the magnitude of the stimulation was lower than in wild-type cells. Thus, these PTKs may participate in the generation of an optimal signal. Notably, an inhibitor of **JAK-3** (Janus family kinase-3) abrogated radiation-induced **c-jun** activation, prompting the hypothesis that a chicken homolog of **JAK-3** may play a key role in initiation of the radiation-induced **c-jun** signal in B-lineage lymphoid cells.

ST gamma irradn **cjun** lymphocyte tyrosine kinase

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**c-jun**; role of tyrosine kinases in induction of **c-jun** proto-oncogene in irradiated B-lineage lymphoid cells)

IT Gamma ray
(irradiation; role of tyrosine kinases in induction of **c-jun** proto-oncogene in irradiated B-lineage lymphoid cells)

IT B cell (lymphocyte)
(role of tyrosine kinases in induction of **c-jun** proto-oncogene in irradiated B-lineage lymphoid cells)

IT **202475-60-3P 211555-04-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(role of tyrosine kinases in induction of **c-jun** proto-oncogene in irradiated B-lineage lymphoid cells)

IT 80449-02-1, Tyrosine kinase 138674-26-7, SYK Tyrosine kinase 140208-17-9, LYN Tyrosine kinase 149147-12-6, Bruton's Tyrosine kinase **157482-36-5**, **JAK-3 kinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(role of tyrosine kinases in induction of **c-jun** proto-oncogene in irradiated B-lineage lymphoid cells)

IT 123-30-8 4998-07-6 16750-67-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(role of tyrosine kinases in induction of **c-jun** proto-oncogene in irradiated B-lineage lymphoid cells)

IT 4959-60-8P 5004-88-6P 13790-39-1P 13794-72-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(role of tyrosine kinases in induction of **c-jun** proto-oncogene in irradiated B-lineage lymphoid cells)

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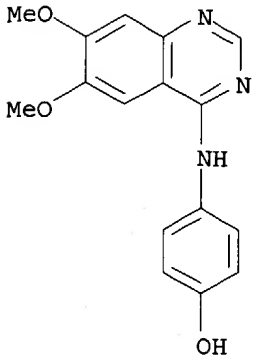
IT **202475-60-3P 211555-04-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(role of tyrosine kinases in induction of **c-jun** proto-oncogene in irradiated B-lineage lymphoid cells)

RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 211555-04-3 HCAPLUS
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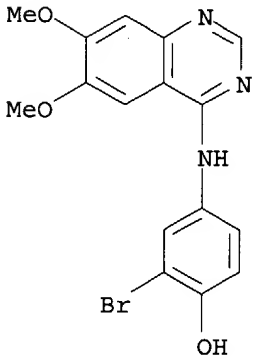

IT **157482-36-5, JAK-3 kinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(role of tyrosine kinases in induction of **c-jun** proto-oncogene in irradiated B-lineage lymphoid cells)
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L55 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:401227 HCAPLUS
DN 129:170172
ED Entered STN: 01 Jul 1998
TI **4-(3'-Bromo-4'hydroxylphenyl)-amino-6,7-dimethoxyquinazoline**: a novel quinazoline derivative with potent cytotoxic activity against human glioblastoma cells
AU Narla, Rama Krishna; Liu, Xing-Ping; Myers, Dorothea E.; **Uckun, Fatih M.**
CS Department of Experimental Oncology, **Hughes Institute**, St. Paul, MN, 55113, USA
SO Clinical Cancer Research (**1998**), 4(6), 1405-1414
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research

DT Journal
LA English
CC 1-6 (Pharmacology)
AB The novel quinazoline derivative **4-(3'-bromo-4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline** (**WHI-P154**) exhibited significant cytotoxicity against U373 and U87 human glioblastoma cell lines, causing apoptotic cell death at micromolar concns. The in vitro antiglioblastoma activity of **WHI-P154** was amplified >200-fold and rendered selective by conjugation to recombinant human epidermal growth factor (EGF). The EGF-P154 conjugate was able to bind to and enter target glioblastoma cells within 10-30 min via receptor (R)-mediated endocytosis by inducing internalization of the EGF-R mols. In vitro treatment with EGF-P154 resulted in killing of glioblastoma cells at nanomolar concns. with an IC50 of 813 ± 139 nM, whereas no cytotoxicity against EGF-R-neg. leukemia cells was observed, even at concns. as high as 100 μM. The in vivo administration of EGF-P154 resulted in delayed tumor progression and improved tumor-free survival in a severe combined immunodeficient mouse glioblastoma xenograft model. Whereas none of the control mice remained alive tumor-free beyond 33 days (median tumor-free survival, 19 days) and all control mice had tumors that rapidly progressed to reach an average size of >500 mm3 by 58 days, 40% of mice treated for 10 consecutive days with 1 mg/kg/day EGF-P154 remained alive and free of detectable tumors for more than 58 days with a median tumor-free survival of 40 days. The tumors developing in the remaining 60% of the mice never reached a size >50 mm3. Thus, targeting **WHI-P154** to the EGF-R may be useful in the treatment of glioblastoma multiforme.
ST quinazoline deriv WHIP154 glioblastoma antitumor
IT Drug targeting
(glioblastoma inhibition by quinazoline derivative **WHI-P154** targeting of EGF receptor)
IT Epidermal growth factor receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(glioblastoma inhibition by quinazoline derivative **WHI-P154** targeting of EGF receptor)
IT Neuroglia
(glioblastoma, inhibitors; glioblastoma inhibition by quinazoline derivative **WHI-P154** targeting of EGF receptor)
IT Antitumor agents
(glioblastoma; glioblastoma inhibition by quinazoline derivative **WHI-P154** targeting of EGF receptor)
IT 62229-50-9D, Epidermal growth factor, conjugates with quinazoline derivative
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(glioblastoma inhibition by quinazoline derivative **WHI-P154** targeting of EGF receptor)
IT **21561-09-1P 153436-54-5P 202475-60-3P 211555-04-3P 211555-05-4P 211555-06-5P 211555-07-6P 211555-08-7P 211555-09-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(glioblastoma inhibition by quinazoline derivative **WHI-P154** targeting of EGF receptor)
IT 13790-39-1P, 4-Chloro-6,7-dimethoxyquinazoline
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(glioblastoma inhibition by quinazoline derivative **WHI-P154** targeting of EGF receptor)
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD

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211555-04-3P 211555-05-4P 211555-06-5P
211555-07-6P 211555-08-7P 211555-09-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(glioblastoma inhibition by quinazoline derivative **WHI-P154** targeting of EGF receptor)

RN 21561-09-1 HCAPLUS
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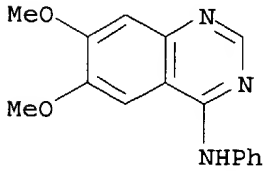

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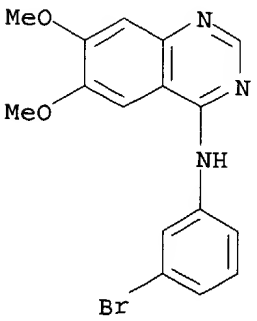

RN 202475-60-3 HCAPLUS

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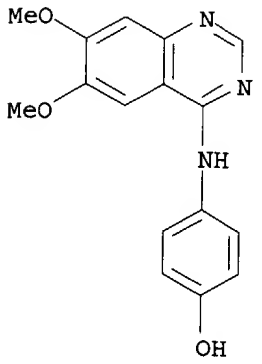

RN 211555-04-3 HCAPLUS
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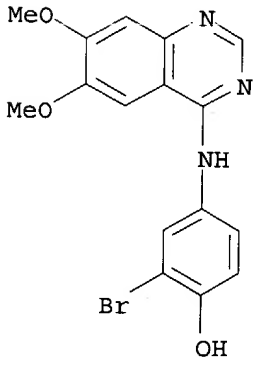

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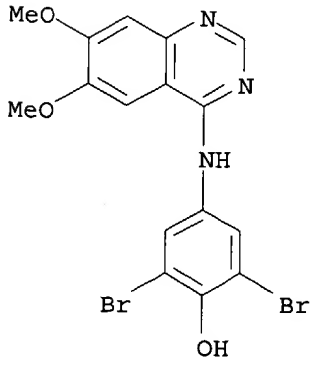

RN 211555-06-5 HCAPLUS
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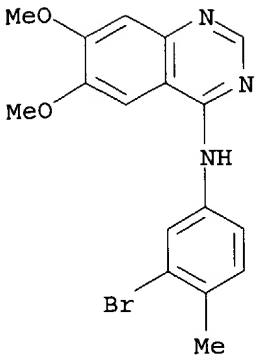

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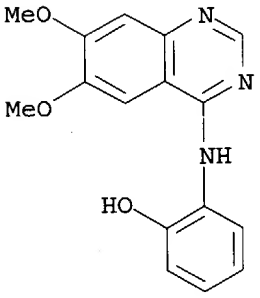

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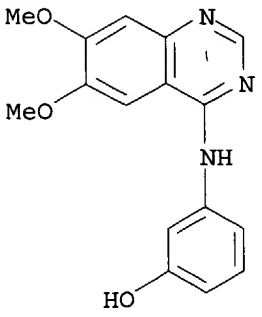

RN 211555-09-8 HCAPLUS
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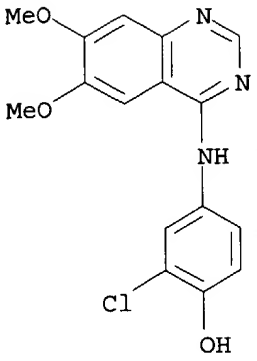


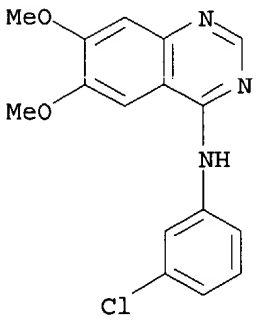
L55 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:116898 HCAPLUS
DN 124:249905
ED Entered STN: 24 Feb 1996
TI Inhibition of acute lymphoblastic leukemia by a **Jak**-2 inhibitor
AU Meydan, Naftaly; Grunberger, Tom; Dadi, Harjit; Shahar, Michal; Arpaia, Enrico; Lapidot, Zvi; Leeder, J. Steven; Freedman, Melvin; Cohen, Amos; et al.
CS The Hospital for Sick Children, Univ. Toronto, Toronto, M5G 1X8, Can.
SO Nature (London) (**1996**), 379(6566), 645-8
CODEN: NATUAS; ISSN: 0028-0836
PB Macmillan Magazines
DT Journal
LA English
CC 1-6 (Pharmacology)
AB Acute lymphoblastic leukemia (ALL) is the most common cancer of childhood. Despite the progress achieved in its treatment, 20% of cases relapse and no longer respond to chemotherapy. The most common phenotype of all cells share surface antigens with very early precursors of B cells and are therefore believed to originate from this lineage. Characterization of the growth requirement of ALL cells indicated that they were dependent on various cytokines, suggesting paracrine and/or autocrine growth regulation. Because many cytokines induce tyrosine phosphorylation in lymphoid progenitor cells, and constitutive tyrosine phosphorylation is commonly observed in B-lineage leukemias, attempts have been made to develop protein tyrosine kinase (PTK) blockers of leukemia cell growth. Here the authors show that leukemic cells from patients in relapse have constitutively activated **Jak**-2 PTK. Inhibition of **Jak**-2 activity by a specific tyrosine kinase blocker, AG-490, selectively blocks leukemic cell growth in vitro and in vivo by inducing programmed cell death, with no deleterious effect on normal hematopoiesis. None of the other tyrphostins tested had any activity against leukemic cells.
ST leukemia **Jak2** protein tyrosine kinase inhibitor; AG490 leukemia **Jak2** protein tyrosine kinase; tyrphostin leukemia inhibitor **Jak2** protein kinase
IT Neoplasm inhibitors
(acute lymphocytic leukemia, inhibition of acute lymphoblastic leukemia by a **Jak**-2 protein tyrosine kinase inhibitor AG-490 in relation to screening of other tyrphostins)
IT 71897-07-9, AG 1295 118409-57-7, AG 18 118409-62-4, AG 126
122520-79-0, AG 30 122520-91-6, AG 294 133550-30-8, AG 490
134036-53-6, AG 370 148741-30-4, AG 879 148741-32-6, AG 1007
153150-84-6, AG 1112 **153436-53-4**, AG 1478 175178-83-3, AG 574
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibition of acute lymphoblastic leukemia by a **Jak**-2 protein tyrosine kinase inhibitor AG-490 in relation to screening of other tyrphostins)

IT **152478-57-4**, **Jak**-2 protein tyrosine kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibition of acute lymphoblastic leukemia by a **Jak**-2 protein tyrosine kinase inhibitor AG-490 in relation to screening of other tyrphostins)

IT **153436-53-4**, AG 1478
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of acute lymphoblastic leukemia by a **Jak**-2 protein tyrosine kinase inhibitor AG-490 in relation to screening of other tyrphostins)

RN 153436-53-4 HCAPLUS
CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



IT **152478-57-4**, **Jak**-2 protein tyrosine kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibition of acute lymphoblastic leukemia by a **Jak**-2 protein tyrosine kinase inhibitor AG-490 in relation to screening of other tyrphostins)

RN 152478-57-4 HCAPLUS
CN Kinase (phosphorylating), JAK2 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d his l56-

(FILE 'REGISTRY' ENTERED AT 13:06:05 ON 08 MAY 2004)

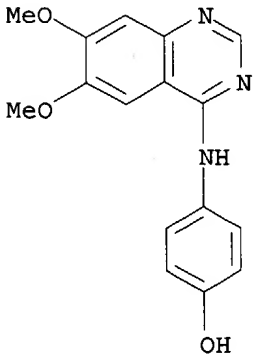
FILE 'HCAPLUS' ENTERED AT 13:06:43 ON 08 MAY 2004
L56 31 S L23 NOT L55
L57 21 S L56 AND (L47-L49 OR CJUN OR C(A)JUN OR JAK# OR JAK 3)
L58 31 S L56,L57

=> => d l58 bib abs hitstr retable tot

L58 ANSWER 1 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:849528 HCAPLUS
DN 140:174738
TI Prevention of islet allograft rejection in diabetic mice by targeting **janus kinase 3** with **4**-(**4**'-**hydroxyphenyl**)-**amino**-**6**,**7**-

dimethoxyquinazoline (JANEX-1)
AU Cetkovic-Cvrlje, Marina; Dragt, Angela L.; **Uckun, Fatih M.**
CS Department of Immunology, Parker **Hughes Institute** and Parker **Hughes** Cancer Center, St. Paul, MN, USA
SO Arzneimittel-Forschung (2003), 53(9), 648-654
CODEN: ARZNAD; ISSN: 0004-4172
PB Editio Cantor Verlag
DT Journal
LA English
AB Janus kinase (**JAK**) **3**-deficient mice were not able to reject allogeneic islet allografts. The **JAK3** inhibitor **4-(4'-hydroxyphenyl)-amino-6,7-dimethoxyquinazoline** (CAS **202475-60-3**, JANEX-1, WHIP131) prevented the rejection of islet allografts in mice with a normal **JAK3** expression status. The combination of JANEX-1 and cyclosporin A (CAS 59865-13-3) was more effective than either agent alone.
IT **157482-36-5**, **Janus kinase 3**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prevention of islet allograft rejection in diabetic mice by targeting **janus kinase 3** with **4-(4'-hydroxyphenyl)-amino-6,7-dimethoxyquinazoline** (JANEX-1))
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **202475-60-3**, JANEX-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prevention of islet allograft rejection in diabetic mice by targeting **janus kinase 3** with **4-(4'-hydroxyphenyl)-amino-6,7-dimethoxyquinazoline** (JANEX-1))
RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RETABLE

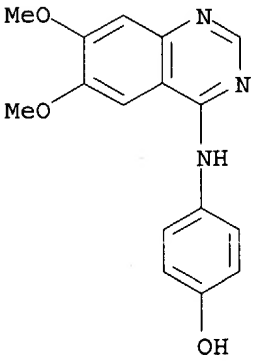
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Boker, A	2001	25	481	World J Surg	MEDLINE
Bretzel, R	2001	109	S384	Exp Clin Endocrinol	HCAPLUS
Bridgett, M	1998	47	1848	Diabetes	HCAPLUS
Cao, X	1995	2	223	Immunity	HCAPLUS
Cetkovic-Cvrlje, M	2001	98	1607	Blood	HCAPLUS
Cetkovic-Cvrlje, M	1997	46	1975	Diabetes	HCAPLUS
Disanto, J	1995	92	377	Proc Natl Acad Sci U	HCAPLUS

Guo, Z	1997	63	716	Transplantation	HCAPLUS
Hall, B	1991	51	1141	Transplantation	MEDLINE
Ihle, J	1995	11	69	Trends Genet	HCAPLUS
Kaplan, H	1996	382	174	Nature	
Kaplan, M	1996	4	313	Immunity	HCAPLUS
Kishimoto, K	2000	106	63	J Clin Invest	HCAPLUS
Koglin, J	2000	101	1034	Circulation	HCAPLUS
Leonard, W	1998	16	293	Annu Rev Immunol	HCAPLUS
Li, X	1998	161	2241	J Immunol	HCAPLUS
Li, X	1998	161	890	J Immunol	HCAPLUS
Mueller, R	1997	159	1599	J Immunol	HCAPLUS
Nikolic, B	2000	105	1289	J Clin Invest	HCAPLUS
Nosaka, T	1995	270	800	Science	HCAPLUS
Park, S	1995	3	771	Immunity	HCAPLUS
Piccotti, R	1997	63	619	Transplantation	
Shapiro, A	2000	343	230	N Engl J Med	HCAPLUS
Shapiro, J	2001	15	241	Best Pract Res Clin	
Shimoda, K	1996	380	630	Nature	HCAPLUS
Strom, T	1996	8	688	Curr Opin Immunol	HCAPLUS
Sudbeck, E	1999	5	1569	Clin Cancer Res	HCAPLUS
Sugamura, K	1996	14	179	Annu Rev Immunol	HCAPLUS
Sutherland, D	2001	25	487	World J Surg	MEDLINE
Takeda, K	1996	380	627	Nature	HCAPLUS
Thierfelder, W	1996	382	171	Nature	HCAPLUS
Thomis, D	1999	163	5411	J Immunol	HCAPLUS
Thomis, D	1995	270	794	Science	HCAPLUS
Tomita, K	2001	276	25378	J Biol Chem	HCAPLUS
Uckun, F	2002	99	4192	Blood	HCAPLUS
Uckun, F	1999	5	2954	Clin Cancer Res	HCAPLUS
Yun, S	2000	69	2480	Transplantation	

L58 ANSWER 2 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:293677 HCAPLUS
DN 139:301736
TI Targeting **JAK3** with JANEX-1 for prevention of autoimmune type 1 diabetes in NOD mice
AU Cetkovic-Cvrlje, Marina; Dragt, Angela L.; Vassilev, Alexei; Liu, Xing-Ping; **Uckun, Fatih M.**
CS Department of Immunology, Parker **Hughes Institute**, St. Paul, MN, 55113, USA
SO Clinical Immunology (San Diego, CA, United States) (2003), 106(3), 213-225
CODEN: CLIIFY; ISSN: 1521-6616
PB Elsevier Science
DT Journal
LA English
AB Here we show that Janus kinase (**JAK**) **3** is an important mol. target for treatment of autoimmune insulin-dependent (type 1) diabetes mellitus. The rationally designed **JAK3** inhibitor JANEX-1 exhibited potent immunomodulatory activity and delayed the onset of diabetes in the NOD mouse model of autoimmune type 1 diabetes. Whereas 60% of vehicle-treated control NOD mice became diabetic by 25 wk, the incidence of diabetes at 25 wk was only 9% for NOD females treated with daily injections of JANEX-1 (100 mg/kg/day) from Week 10 through Week 25 ($P = 0.007$). Furthermore, JANEX-1 prevented the development of insulitis and diabetes in NOD-scid/scid females after adoptive transfer of splenocytes from diabetic NOD females. Chemical inhibitors such as JANEX-1 may provide the basis for effective treatment modalities against human type 1 diabetes. To our knowledge, this is the first report of the immunosuppressive activity of a **JAK3** inhibitor in the context of an autoimmune disease.
IT **157482-36-5**, **Janus kinase 3**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(JANEX-1 prevention of autoimmune type 1 diabetes mediated by

JAK3)
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **202475-60-3P**, JANEX 1
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(JANEX-1 prevention of autoimmune type 1 diabetes mediated by **JAK3**)
RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



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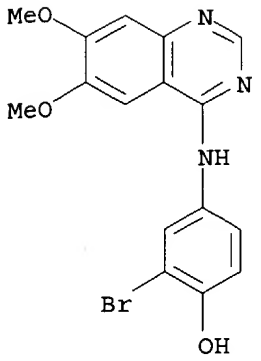
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Akdis, C	2001	103	131	Immunology	HCAPLUS
Bach, J	2001	19	131	Annu Rev Immunol	HCAPLUS
Baeder, W	1992	89	174	Clin Exp Immunol	HCAPLUS
Bowman, M	1994	15	115	Immunol Today	HCAPLUS
Bridgett, M	1998	47	1848	Diabetes	HCAPLUS
Cao, X	1995	2	223	Immunity	HCAPLUS
Cetkovic-Cvrlje, M	2001	98	1607	Blood	HCAPLUS
Cetkovic-Cvrlje, M	1997	46	1975	Diabetes	HCAPLUS
Cetkovic-Cvrlje, M	2001	50	A410	Diabetes	
DiSanto, J	1995	92	377	Proc Natl Acad Sci U	HCAPLUS
Formby, B	1987	241	1106	J Pharm Exp Ther	HCAPLUS
Greiner, D	2001	100	134	Clin Immunol	HCAPLUS
Gross, D	1994	37	1195	Diabetologia	HCAPLUS
Groux, H	1996	184	1	J Exp Med	
Hanson, M	1996	157	1279	J Immunol	HCAPLUS
Hsu, D	1990	250	830	Science	HCAPLUS
Ihle, J	1995	11	69	Trends Genet	HCAPLUS
Kai, N	1993	55	936	Transplantation	HCAPLUS
Kikutani, H	1992	51	285	Adv Immunol	HCAPLUS
Lee, L	1999	190	1263	J Exp Med	
Leonard, W	1998	16	293	Annu Rev Immunol	HCAPLUS
Li, X	2000	164	1193	J Immunol	HCAPLUS
Mahajan, S	2001	276	31216	J Biol Chem	HCAPLUS
Mahon, J	1993	696	351	Ann NY Acad Sci	MEDLINE
Mathieu, C	1992	41	1491	Diabetes	HCAPLUS
Mathieu, C	1995	136	866	Endocrinology	HCAPLUS
Min, D	1991	11	119S	Pharmacotherapy	MEDLINE
Mori, Y	1986	29	244	Diabetologia	HCAPLUS
Moritani, M	1996	98	1851	J Clin Invest	HCAPLUS

Nosaka, T	1995	270	800	Science	HCAPLUS
Park, S	1995	3	771	Immunity	HCAPLUS
Pennline, K	1994	71	169	Clin Immunol Immunop	HCAPLUS
Philips, J	2001	167	6087	J Immunol	
Rabinovitch, A	2002	51	638	Diabetes	HCAPLUS
Rabinovitch, A	1998	14	129	Diabetes Metab Rev	HCAPLUS
Ramiya, V	1996	9	349	J Autoimmun	MEDLINE
Rossini, A	1995	74	2	Clin Immunol Immunop	HCAPLUS
Saemann, M	2000	70	1215	Transplantation	HCAPLUS
Sudbeck, E	1999	5	1569	Clin Cancer Res	HCAPLUS
Thomas, H	2000	16	251	Diabetes Metabolism	MEDLINE
Thomis, D	1999	163	5411	J Immunol	HCAPLUS
Thomis, D	1995	270	794	Science	HCAPLUS
Tomita, K	2001	276	25378	J Biol Chem	HCAPLUS
Uckun, F	2002	99	4192	Blood	HCAPLUS
Uckun, F	1999	5	2954	Clin Cancer Res	HCAPLUS
Uckun, F	2003			Drug Res in press	
Wang, L	2000	95	3816	Blood	HCAPLUS
Wong, S	1999	13	290	J Autoimmunity	
Yang, Z	2002	168	6479	J Immunol	HCAPLUS
Yoshida, K	2000	2	140	Rev Immunogenet	MEDLINE
Zaccone, P	1999	48	1522	Diabetes	HCAPLUS
Zheng, X	1997	158	4507	J Immunol	HCAPLUS

L58 ANSWER 3 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:694236 HCAPLUS
DN 138:248178
TI Augmentation of mast cell bactericidal activity by the anti-leukemic drug, **4-(3'-bromo-4'-hydroxylphenyl)amino-6,7-dimethoxyquinazoline**
AU Malaviya, Ravi; Navara, Christopher; **Uckun, Fatih M.**
CS Department of Allergy and Inflammatory Diseases, Parker **Hughes** Cancer Center, St. Paul, MN, 55113, USA
SO Leukemia & Lymphoma (2002), 43(6), 1329-1332
CODEN: LELYEA; ISSN: 1042-8194
PB Taylor & Francis Ltd.
DT Journal
LA English
AB Mast cells play a pivotal role in host innate immune defense against gram neg. bacterial infections by killing gram neg. bacteria and recruiting neutrophils to the sites of active infection through the release of TNFα and leukotrienes. Here, we report that the antileukemic compound **4-(3'-bromo-4'-hydroxylphenyl)amino-6,7-dimethoxyquinazoline**, designated as MASTPROM, augments the bactericidal activity of mast cells by increasing the binding of bacteria to and their phagocytosis by mast cells. MASTPROM also promoted the bacterial clearance in a mouse model of bacterial peritonitis. MASTPROM may provide the basis for novel supportive care regimens aimed at augmenting the bactericidal activity of mast cells and thereby potentiating the innate immune response against gram neg. organisms.
IT **211555-04-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(augmentation of mast cell bactericidal activity by the antileukemic drug, (bromohydroxylphenyl)aminodimethoxyquinazoline)
RN 211555-04-3 HCAPLUS
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Barriere, S	1995	23	376	Crit Care Med	MEDLINE
Echtenacher, B	1996	381	75	Nature	HCAPLUS
Firsov, A	1998	42	2848	Antimicrob Agents Ch	HCAPLUS
Malaviya, R	1999	257	807	Biochem Biophys Res	HCAPLUS
Malaviya, R	1993	268	4939	J Biol Chem	HCAPLUS
Malaviya, R	1994	93	1645	J Clin Investig	MEDLINE
Malaviya, R	1994	152	1907	J Immunol	HCAPLUS
Malaviya, R	2000	67	841	J Leukoc Biol	HCAPLUS
Malaviya, R	1995	253	27	Methods Enzymol	MEDLINE
Malaviya, R	1996	381	77	Nature	HCAPLUS
Malaviya, R	1999	96	8110	Proc Natl Acad Sci U	HCAPLUS
Qureshi, R	1988	141	2090	J Immunol	MEDLINE
Schifferli, D	1988	32	1609	Antimicrob Agents Ch	HCAPLUS
Sher, A	1983	131	1460	J Immunol	MEDLINE
Sher, A	1979	41	490	Lab Investig	MEDLINE
Sher, A	1976	263	334	Nature	MEDLINE
Sudbeck, E	1999	5	1569	Clin Cancer Res	HCAPLUS
Tewari, R	1993	268	3009	J Biol Chem	HCAPLUS
Uckun, F	2000			US 6066640 A	
van den Broek, P	1989	11	213	Rev Infect Dis	HCAPLUS
Xu, L	1993	45	385	Prostaglandins	HCAPLUS

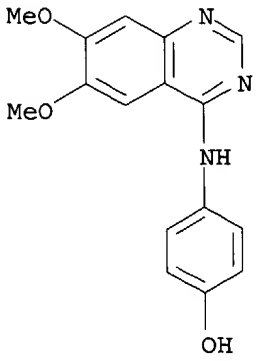
L58 ANSWER 4 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:418844 HCAPLUS
DN 137:320073
TI **Janus kinase 3** inhibitor **WHI-P131**/JANEX-1 prevents graft-versus-host disease but spares the graft-versus-leukemia function of the bone marrow allografts in a murine bone marrow transplantation model
AU **Uckun, Fatih M.**; Roers, Bertram A.; Waurzyniak, Barbara; Liu, Xing-Ping; Cetkovic-Cvrlje, Marina
CS Experimental BMT Program, Parker **Hughes** Cancer Center and Departments of Immunology, Pathology, Chemistry, Parker **Hughes Institute**, St Paul, MN, USA
SO Blood (2002), 99(11), 4192-4199
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB The purpose of the present study was to evaluate the effects of graft-vs.-host disease (GVHD) prophylaxis with the **Janus kinase 3** (**JAK3**) inhibitor **WHI-P131**/JANEX-1 on the graft-vs.-leukemic (GVL) function of marrow

allografts in mice undergoing bone marrow transplantation (BMT) after being challenged with an otherwise invariably fatal dose of BCL-1 leukemia cells. GVHD prophylaxis using **WHI-P131** markedly improved the survival outcome after BMT. The probability of survival at 30 days after BMT was 11% ± 6% for vehicle-treated recipients (median survival time, 25 days) vs. 63% ± 12% for recipients treated with **WHI-P131** (median survival time, 36 days; P <.0001). Because **WHI-P131** is devoid of antileukemic activity against BCL-1 leukemia cells, this marked improvement in survival outcome was due to reduced incidence of GVHD-associated fatalities combined with sustained GVL function of the allografts in the **WHI-P131** group. Notably, adoptive transfer expts. demonstrated that the spleens of **WHI-P131**-treated allograft recipients contained less than 0.001% BCL-1 cells. Notably, GVHD prophylaxis with **WHI-P131** plus methotrexate resulted in 100% survival of mice receiving allotransplants challenged with an otherwise invariably fatal dose of BCL-1 leukemia. Taken together, our results provide strong exptl. evidence that GVHD prophylaxis using **WHI-P131** does not impair the GVL function of the allografts and consequently contributes to an improved post-BMT survival outcome of the recipient mice.

IT **157482-36-5, Janus kinase 3**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**Janus kinase 3** inhibitor **WHI-P131**/JANEX-1 prevents graft-vs.-host disease but spares the graft-vs.-leukemia function of the bone marrow allografts in a murine bone marrow transplantation model)
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **202475-60-3, WHI-P131**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**Janus kinase 3** inhibitor **WHI-P131**/JANEX-1 prevents graft-vs.-host disease but spares the graft-vs.-leukemia function of the bone marrow allografts in a murine bone marrow transplantation model)
RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Apperly, J	1986	1	53	Bone Marrow Transpla	
Berenson, R	1996	14	589	Cancer Invest	MEDLINE
Butturini, A	1994	1	402	Curr Opin Hematol	MEDLINE

Cetkovic-Cvrlje, M	2001	98	1607	Blood	HCAPLUS
Champlin, R	1999		413	Hematology, ASH Educ	
Henslee-Downey, P	1995	7	115	Curr Opin Oncol	MEDLINE
Krolick, K	1979	123	1928	J Immunol	MEDLINE
Leelasiri, A	1995	15	401	Bone Marrow Transpla	MEDLINE
Marmont, A	1991	78	2120	Blood	MEDLINE
Martin, P	1988	3	445	Bone Marrow Transpla	MEDLINE
Orchard, P	1998	22	201	Bone Marrow Transpla	MEDLINE
O'Reilly, R	1997	1		Allogeneic Transplan	
Porter, D	1999	5	253	Biol Blood Marrow Tr	MEDLINE
Poynton, C	1988	3	265	Bone Marrow Transpla	MEDLINE
Ramsay, N	1990	75	815	Blood	MEDLINE
Slavin, S	1981	41	4162	Cancer Res	MEDLINE
Slavin, S	2001	39	25	Crit Rev Oncol Hemat	MEDLINE
Slavin, S	1978	272	624	Nature	MEDLINE
Spitzer, T	2000	6	309	Biol Blood Marrow Tr	MEDLINE
Sudbeck, E	1999	5	1569	Clin Cancer Res	HCAPLUS
Thomas, E	1997	45	1	Arch Immunol Ther Ex	MEDLINE
Trigg, M	1988	35	933	Pediatr Clin North A	MEDLINE
Uckun, F	1992	15	2649	Blood	
Uckun, F	1999	5	2954	Clin Cancer Res	HCAPLUS
Waddick, K	1995	19	121	Leuk Lymphoma	MEDLINE

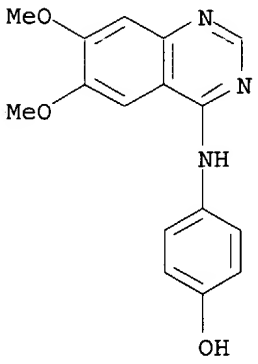
L58 ANSWER 5 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:12295 HCAPLUS
DN 136:272618
TI CYP1A-mediated metabolism of the **Janus kinase-3** inhibitor **4-(4'-hydroxyphenyl)-amino-6,7-dimethoxyquinazoline**: structural basis for inactivation by regioselective O-demethylation
AU **Uckun, Fatih M.**; Thoen, Jason; Chen, Hao; Sudbeck, Elise; Mao, Chen; Malaviya, Ravi; Liu, Xing-Ping; Chen, Chun-Lin
CS Departments of Pharmaceutical Sciences, Drug Discovery Program, Parker **Hughes** Cancer Center, St. Paul, MN, 55113, USA
SO Drug Metabolism and Disposition (2002), 30(1), 74-85
CODEN: DMDSAI; ISSN: 0090-9556
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Here the authors report the phase I metabolism of the rationally designed **Janus kinase-3** (**JAK**) inhibitor **4-(4'-hydroxyphenyl)-amino-6,7-dimethoxyquinazoline** (**WHI-P131**; JANEX-1). JANEX-1 was metabolized by the cytochrome P 450 enzymes CYP1A1 and CYP1A2 in a regioselective fashion to form the biol. inactive 7-O-demethylation product 4-(4'-hydroxyphenyl)-amino-6-methoxy-7-hydroxyquinazoline (JANEX-1-M). Our mol. modeling studies indicated that the CYP1A family enzymes bind and demethylate JANEX-1 at the C-7 position of the quinazoline ring since the alternative binding conformation with demethylation at the C-6 position would result in a severe steric clash with the binding site residues. The metabolism of JANEX-1 to JANEX-1-M in pooled human liver microsomes followed Michaelis-Menten kinetics with Vmax and Km values of 34.6 pmol/min/mg and 107.3 μM, resp. α-Naphthoflavone and furafylline, which both inhibit CYP1A2, significantly inhibited the formation of JANEX-1-M in human liver microsomes. There was a direct correlation between CYP1A activities and the magnitude of JANEX-1-M formation in the liver microsomes from different animal species. A significantly increased metabolic rate for JANEX-1 was observed in Aroclor 1254-, β-naphthoflavone-, and 3-methylcholanthrene-induced microsomes but not in clofibrate-, dexamethasone-, isoniazid-, and phenobarbital-induced microsomes. The formation of JANEX-1-M in the presence of baculovirus-expressed CYP1A1 and 1A2 was consistent with Michaelis-Menten kinetics. The systemic clearance

of JANEX-1-M was much faster than that of JANEX-1 (5525.1 mL/h/kg vs. 1458.0 mL/h/kg). Consequently, the area under the curve value for JANEX-1-M was much smaller than that for JANEX-1 (27.5 vs. 94.8 μM · h).

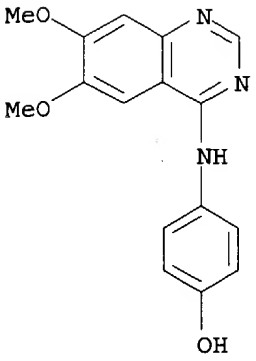
IT **157482-36-5, Janus kinase 3**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CYP1A-mediated metabolism of **Janus kinase-3** inhibitor 4'-hydroxyphenyl-aminodimethoxyquinazoline and structural basis for inactivation by regioselective O-demethylation)
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **202475-60-3, WHI-P131**
RL: PKT (Pharmacokinetics); PRP (Properties); BIOL (Biological study)
(CYP1A-mediated metabolism of **Janus kinase-3** inhibitor 4'-hydroxyphenyl-aminodimethoxyquinazoline and structural basis for inactivation by regioselective O-demethylation)
RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **188829-39-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(CYP1A-mediated metabolism of **Janus kinase-3** inhibitor 4'-hydroxyphenyl-aminodimethoxyquinazoline and structural basis for inactivation by regioselective O-demethylation)
RN 188829-39-2 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Bohm, H	1992	6	593	J Comput-Aided Mol D	MEDLINE
Brunger, A	1992			X-PLOR, a System for	
Cetkovic-Cvrlje, M	2001	98	1607	Blood	HCAPLUS
Chen, C	2001	29	1035	Drug Metab Dispos	HCAPLUS
Chen, C	1995	20	151	Eur J Drug Metab Pha	HCAPLUS
Chen, C	1999	727	205	J Chromatogr B	HCAPLUS
Chen, C	1999	16	1003	Pharm Res	HCAPLUS
Crespi, C	1995	26	180	Adv Drug Res	
Davies, B	1993	10	1093	Pharm Res	MEDLINE
Galli, S	1993	328	257	New Eng J Med	MEDLINE
Goodman, P	1998	273	17742	J Biol Chem	HCAPLUS
Grange, J	1994	11	242	Drug Safety	HCAPLUS
Hasemann, C	1994	236	1169	J Mol Biology	HCAPLUS
Hishiki, T	2000	128	965	J Biochem	HCAPLUS
Kajita, J	2000	28	1121	Drug Metab Dispos	HCAPLUS
Kaye, B	1986	21	19S	Br J Clin Pharmacol	HCAPLUS
Kronbach, T	1989	36	89	Mol Pharmacol	HCAPLUS
Malaviya, R	2001	8	35	Am J Ther	
Malaviya, R	1999	257	807	Biochem Biophys Res	HCAPLUS
Malaviya, R	1993	268	4939	J Biol Chem	HCAPLUS
Malaviya, R	1999	274	27028	J Biol Chem	HCAPLUS
Miyajima, I	1997	99	901	J Clin Invest	HCAPLUS
Narla, R	1998	4	2463	Clin Cancer Res	HCAPLUS
Oettgen, H	1994	370	367	Nature (Lond)	HCAPLUS
Ozawa, K	1993	268	1749	J Biol Chem	HCAPLUS
Sack, J	1988	6	244	J Mol Graphics	
Scharenberg, A	1995	14	3385	EMBO (Eur Mol Biol O	HCAPLUS
Sheldrick, G	2001			SADABS 2.03 Program	
Sudbeck, E	2000	56	1282	Acta Crystallogr C	
Sudbeck, E	1998	92	599a	Blood	
Sudbeck, E	1999	5	1569	Clin Cancer Res	HCAPLUS
Taylor, J	1977	7	357	Xenobiotica	HCAPLUS
Tibbles, H	2001	276	17815	J Biol Chem	HCAPLUS
Trieu, V	2000	267	22	Biochem Biophys Res	HCAPLUS
Uckun, F	1999	5	2954	Clin Cancer Res	HCAPLUS
Uckun, F	1999	291	1301	J Pharmacol Exp Ther	HCAPLUS
Waxman, D	1999	369	11	Arch Biochem Biophys	HCAPLUS
Wynalda, M	2000	28	1014	Drug Metab Dispos	MEDLINE
Yamato, C	1982	12	549	Xenobiotica	HCAPLUS

L58 ANSWER 6 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:695080 HCAPLUS
DN 136:4654
TI Targeting **Janus kinase 3** to attenuate the severity of acute graft-versus-host disease across the major histocompatibility barrier in mice
AU Cetkovic-Cvrlje, Marina; Roers, Bertram A.; Waurzyniak, Barbara; Liu, Xing-Ping; **Uckun, Fatih M.**
CS Experimental BMT Program, Parker **Hughes** Cancer Center, Departments of Pathology, Chemistry, Parker **Hughes Institute**, St Paul, MN, 55113, USA
SO Blood (2001), 98(5), 1607-1613
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB To prevent the development of acute graft-vs.-host disease (GVHD) in lethally irradiated C57BL/6 (H-2b) recipient mice transplanted with bone marrow-splenocyte grafts from major histocompatibility complex (MHC) disparate BALB/c mice (H-2d), recipient mice were treated with the rationally designed **JAK3** inhibitor **WHI-P131** [**4-(4'-hydroxyphenyl)-amino-6,7-dimethoxyquinazoline**] (20 mg/kg, 3 times a day [tid]) daily from the day of bone marrow transplantation (BMT) until the end of the 85-day observation period. Total body irradiation (TBI)-conditioned, vehicle-treated control C57BL/6 mice (n = 38) receiving bone marrow-splenocyte grafts from BALB/c mice survived acute TBI toxicity, but they all developed histol. confirmed severe multi-organ GVHD and died after a median survival time of 37 days. **WHI-P131** treatment (20 mg/kg i.p., tid) prolonged the median survival time of the BMT recipients to 56 days. The probability of survival at 2 mo after BMT was 11% ± 5% for vehicle-treated control mice (n = 38) and 41% ± 9% for mice treated with **WHI-P131** (n = 32) (P < .0001). Notably, the combination regimen **WHI-P131** plus the standard anti-GVHD drug methotrexate (MTX) (10 mg/m2 per day) was more effective than **WHI-P131** or MTX alone. More than half the C57BL/6 recipients receiving this most effective GVHD prophylaxis remained alive and healthy throughout the 85-day observation period, with a cumulative survival probability of 70% ± 10%. Taken together, these results indicate that targeting **JAK3** in alloreactive donor lymphocytes with a chemical inhibitor such as **WHI-P131** may attenuate the severity of GVHD after BMT.
IT **157482-36-5, Janus kinase 3**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(targeting **Janus kinase 3** to attenuate the severity of acute graft-vs.-host disease across the major histocompatibility barrier in mice)
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Apperly, J	1986	1	53	Bone Marrow Transpla	
Atkinson, K	1991	21	850	Aust N Z J Med	MEDLINE
Barrett, A	1989	74	862	Blood	MEDLINE
Berenson, R	1996	14	589	Cancer Invest	MEDLINE
Bowman, T	2000	19	2474	Oncogene	HCAPLUS
Bryson, J	1997	19	721	Bone Marrow Transpla	MEDLINE
Buckley, R	1997	130	378	J Pediatr	MEDLINE

Cetkovic-Cvrlje, M	1997	46	1975	Diabeles	HCAPLUS
Clift, R	1990	76	1867	Blood	MEDLINE
Darnell, J	1994	264	1415	Science	HCAPLUS
Deeg, H	1997	89	3880	Blood	HCAPLUS
Dinsmore, R	1983	62	381	Blood	MEDLINE
Grossman, W	1999	94	932	Blood	HCAPLUS
Hanson, M	1996	157	1279	J Immunol	HCAPLUS
Henslee-Downey, P	1995	7	115	Curr Opin Oncol	MEDLINE
Horita, M	2000	191	977	J Exp Med	HCAPLUS
Ihle, J	1995	11	69	Trends Genet	HCAPLUS
Leelasiri, A	1995	15	401	Bone Marrow Transpla	MEDLINE
Levy, D	1997	8	81	Cytokine Growth Fact	HCAPLUS
Marmont, A	1991	78	2120	Blood	MEDLINE
Martin, P	1988	3	445	Bone Marrow Transpla	MEDLINE
Matherly, L	1996	21	359	Leuk Lymphoma	MEDLINE
Miyazaki, T	1996	27	25	Cancer Surv	HCAPLUS
Nosaka, T	1995	270	800	Science	HCAPLUS
O'Reilly, R	1997			Allogeneic Transplan	
O'Reilly, R	1983	62	941	Blood	MEDLINE
Poynton, C	1988	3	265	Bone Marrow Transpla	MEDLINE
Ruulu, T	2000	96	2391	Blood	
Storb, R	1990	76	1037	Blood	MEDLINE
Sudbeck, E	1999	5	1569	Clin Cancer Res	HCAPLUS
Thomas, E	1989	73	861	Blood	MEDLINE
Thomis, D	1995	270	794	Science	HCAPLUS
Uckun, F	1990	76	2449	Blood	MEDLINE
Uckun, F	1999	5	2954	Clin Cancer Res	HCAPLUS
Uckun, F	1988	85	8603	Proc Natl Acad Sci	HCAPLUS
Villa, A	1996	88	817	Blood	HCAPLUS
Wingard, J	1990	8	820	J Clin Oncol	MEDLINE

L58 ANSWER 7 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:472434 HCAPLUS
DN 135:41029
TI **JAK-3** inhibitors and/or inhibitors of STAT-3 phosphorylation for inhibitors of thrombin-induced platelet aggregation
IN **Uckun, Fatih M.**
PA Parker **Hughes Institute**, USA
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001045641	A2	20010628	WO 2000-US42345	20001129
	WO 2001045641	A3	20020912		
	WO 2001045641	C1	20031023		
	W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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	AU 2001049032	A5	20010703	AU 2001-49032	20001129
	JP 2003518023	T2	20030603	JP 2001-546382	20001129
	WO 2002043735	A1	20020606	WO 2001-US2195	20010123
	W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI,				

GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR,
TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,
RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	AU 2001029722	A5	20020611	AU 2001-29722	20010123
	US 2003013728	A1	20030116	US 2002-157474	20020528
	US 6635651	B2	20031021		
	US 2004034045	A1	20040219	US 2003-449408	20030529
PRAI	US 1999-168179P	P	19991130		
	WO 2000-US42345	W	20001129		
	WO 2001-US2195	W	20010123		

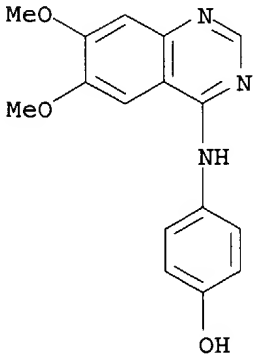
OS MARPAT 135:41029

AB A therapeutic method useful for treating or preventing a condition of platelet aggregation in a subject includes administering a pharmaceutically effective amount of a compound or composition that inhibits **JAK-3** and/or tyrosine phosphorylation of STAT-3 and inhibits thrombin-induced platelet aggregation. The condition of platelet aggregation includes hematopoietic and cerebrovascular diseases.

IT **202475-60-3, WHI-P 131**
211555-04-3, WHI-P 154
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**JAK-3** inhibitors and/or inhibitors of STAT-3 phosphorylation for inhibitors of thrombin-induced platelet aggregation)

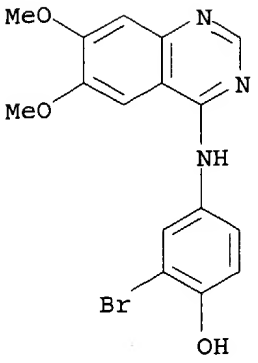
RN 202475-60-3 HCAPLUS

CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 211555-04-3 HCAPLUS

CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **157482-36-5**, **Jak3 kinase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**JAK-3** inhibitors and/or inhibitors of STAT-3 phosphorylation for inhibitors of thrombin-induced platelet aggregation)
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

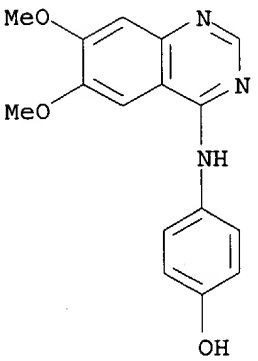
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L58 ANSWER 8 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:434852 HCAPLUS
DN 135:29154
TI Estrogens, especially phytoestrogens, for treating amyotrophic lateral sclerosis (ALS)
IN **Uckun, Fatih M.**; Trieu, Vuong N.; Liu, Xing-Ping
PA Parker **Hughes Institute**, USA
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001041751	A2	20010614	WO 2000-US33194	20001207
	WO 2001041751	A3	20020906		
	WO 2001041751	C1	20031023		
	W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6334998	B1	20020101	US 1999-455846	19991207
	US 2002052385	A1	20020502	US 2001-7967	20011102
	US 6592845	B2	20030715		
PRAI	US 1999-455846	A	19991207		

OS MARPAT 135:29154
AB A method is provided for preventing and treating ALS by administering a phytoestrogen, preferably genistein. Preparation and biol. testing of 2,4,4'-trihydroxydeoxybenzoin are described.
IT **202475-60-3**, **4-(4'-Hydroxyphenyl)**

amino-6,7-dimethoxyquinazoline
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phytoestrogens for treating amyotrophic lateral sclerosis)
RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L58 ANSWER 9 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:424205 HCAPLUS
DN 135:204806
TI Structure-based design of novel anticancer agents
AU **Uckun, F. M.**; Sudbeck, E. A.; Mao, C.; Ghosh, S.; Liu, X.-P.; Vassilev, A. O.; Navara, C. S.; Narla, R. K.
CS Drug Discovery Program, Parker **Hughes** Cancer Center, Parker **Hughes Institute**, St. Paul, MN, 55113, USA
SO Current Cancer Drug Targets (2001), 1(1), 59-71
CODEN: CCDTB9; ISSN: 1568-0096
PB Bentham Science Publishers Ltd.
DT Journal; General Review
LA English
AB A review with 123 refs. Recently identified agents that interact with cytoskeletal elements such as tubulin include synthetic spiroketal pyrans (SPIKET) and monotetrahydrofuran compds. (COBRA compds.). SPIKET compds. target the spongistatin binding site of β-tubulin and COBRA compds. target a unique binding cavity on α-tubulin. At nanomolar concns., the SPIKET compound SPIKET-P causes tubulin depolymn. and exhibits potent cytotoxic activity against cancer cells. COBRA-1 inhibits GTP-induced tubulin polymerization Treatment of human breast cancer and brain tumor cells with COBRA-1 caused destruction of microtubule organization and apoptosis. Other studies have identified some promising protein tyrosine kinase inhibitors as anti-cancer agents. These include EGFR inhibitors such as the quinazoline derivative WHI-P97 and the leflunomide metabolite analog LFM-A12. Both LFM-A12 and WHI-P97 inhibit the in vitro invasiveness of EGFR pos. human breast cancer cells at micromolar concns. and induce apoptotic cell death. Dimethoxyquinazoline compds. **WHI-P131** and **WHI-P154** inhibit tyrosine kinase **JAK3** in leukemia cells. Of particular interest is **WHI-P131**, which inhibits **JAK3** but not **JAK1**, **JAK2**, SYK, BTK, LYN, or IRK at concns. as high as 350 μM. Studies of BTK inhibitors showed that the leflunomide metabolite analog LFM-A13 inhibited BTK in leukemia and lymphoma cells. Consistent with the anti-apoptotic function of BTK, treatment of leukemic cells with LFM-A13 enhanced their sensitivity to chemotherapy-induced apoptosis.
IT **161384-16-3**, Janus kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitors; structure-based design of novel anticancer agents)
RN 161384-16-3 HCAPLUS
CN Kinase (phosphorylating), JAK protein (9CI) (CA INDEX NAME)

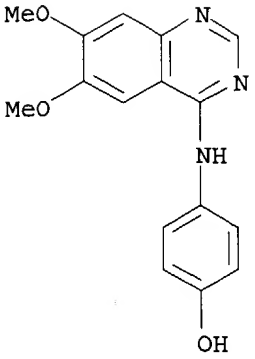
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Akiyama, T	1987	262	5592	J Biol Chem	HCAPLUS
Anderson, J	1996	93	10966	Proc Natl Acad Sci U	HCAPLUS
Avila, J	1992	50	327	Life Sci	HCAPLUS
Bai, R	1990	39	1941	Biochem Pharmacol	HCAPLUS
Bai, R	1995	34	9714	Biochemistry	HCAPLUS
Bai, R	1993	44	757	Molecular Pharmacolo	HCAPLUS
Begemann, M	1996	2	1017	Clin Cancer Res	HCAPLUS
Bollag, D	1995	55	2325	Cancer Res	HCAPLUS
Bridges, A	1996	39	267	Med Chem	HCAPLUS
Caravatti, G	1994	4	399	Bioorg Med Chem Lett	HCAPLUS
Carpenter, G	1990	265	7709	J Biol Chem	HCAPLUS
Chae, H	1993	53	447	Cancer Res	HCAPLUS
Chrysogelos, S	1994	29	29	Breast Cancer Resear	MEDLINE
Derry, W	1997	36	3554	Biochemistry	HCAPLUS
Derry, W	1998	58	1177	Cancer Res	HCAPLUS
Desai, A	1997	13	83	Annu Rev Cell Dev Bi	HCAPLUS
Dionne, C	1998	4	1887	Clin Cancer Res	HCAPLUS
Downing, K	1998	10	16	Curr Opin Cell Biol	HCAPLUS
Erickson, H	1995	80	367	Cell	HCAPLUS
Fiorucci, G	1995	69	5833	J Virol	HCAPLUS
Fox, S	1994	29	41	Breast Cancer Res Tr	MEDLINE
Fry, D	1998	95	12022	Proc Natl Acad Sci U	HCAPLUS
Fry, D	1994	265	1093	Science	HCAPLUS
Fujita-Yamaguchi, Y	1988	157	955	Biochem Biophys Res	HCAPLUS
George-Nascimento, C	1988	27	797	Biochemistry	HCAPLUS
Ghosh, S	1999	55	1364	Acta Crystallogr C	
Ghosh, S	1999	14	403	Anticancer Drug Desi	HCAPLUS
Ghosh, S	1998	4	2657	Clin Can Res	HCAPLUS
Ghosh, S	1999	5	4264	Clin Can Res	HCAPLUS
Goodman, P	1998	273	17742	J Biol Chem	HCAPLUS
Haldar, S	1996	56	1253	Cancer Res	HCAPLUS
Harpur, A	1992	7	1347	Oncogene	HCAPLUS
Huang, H	2000	41	1699	Tet Lett	HCAPLUS
Hubbard, S	1997	16	5572	The E M B O Journal	HCAPLUS
Hyams, J	1994			Microtubules	
Hyman, A	1998	111	2077	J Cell Sci	
Ido, M	1986	10	1063	Leuk Res	HCAPLUS
Jan, S	1999	40	193	Tet Lett	HCAPLUS
Jiang, J	1998	58	5389	Cancer Res	HCAPLUS
Jordan, A	1998	18	259	Med Res Rev	HCAPLUS
Karin, M	1997	9	240	Curr Opin Cell Biol	HCAPLUS
Kawakami, Y	1999	96	2227	Proc Natl Acad Sci U	HCAPLUS
Kawamoto, S	1984	125	258	Biochem Biophys Res	HCAPLUS
Kerksiek, K	1995	377	59	FEBS Lett	HCAPLUS
Kerner, J	1995	3	301	Immunity	HCAPLUS
Khazaie, K	1993	12	255	Cancer & Metasis Rev	HCAPLUS
Kozielski, F	1998	8	191	Curr Biol	HCAPLUS
Krolewski, J	1990	5	277	Oncogene	HCAPLUS
Krystal, G	1998	58	4660	Cancer Res	HCAPLUS
Kurosaki, T	1997	9	309	Curr Opin Immunol	HCAPLUS
Lamers, M	1999	285	713	J Mol Biol	HCAPLUS
Lee, L	1998	273	28253	J Biol Chem	HCAPLUS
Levy, D	1997	8	81	Cytokine Growth Fact	HCAPLUS
Liu, K	1998	10	271	Curr Opin Immunol	HCAPLUS

Mahajan, S	1999	274	9587	J Biol Chem	HCAPLUS
Malaviya, R	1999	257	807	Biochem Biophys Res	HCAPLUS
Manna, S	1999	162	2095	J Immunol	HCAPLUS
Mathe, G	1985	27	285	Cancer Lett	MEDLINE
Mattar, T	1993	334	161	FEBS Lett	HCAPLUS
McCloskey, D	1996		847	Clin Cancer Res	HCAPLUS
Meggio, F	1995	234	317	Eur J Biochem	HCAPLUS
Mendelsohn, J	1995		607	Antibodies to growth	
Merritt, J	1999	43	371	Cancer Chemother Pha	HCAPLUS
Meydan, N	1996	379	645	Nature	HCAPLUS
Miknyoczki, S	1999	880	252	Ann N Y Acad Sci	HCAPLUS
Miknyoczki, S	1999	5	2205	Clin Cancer Res	HCAPLUS
Moyer, J	1997	57	4838	Cancer Res	HCAPLUS
Myers, D	1995	92	9575	Proc Natl Acad Sci U	HCAPLUS
Nakano, H	1987	40	706	J Antibiot	HCAPLUS
Narla, R	1998	4	2463	Clin Cancer Res	HCAPLUS
Nielsen, M	1997	94	6764	Proc Natl Acad Sci U	HCAPLUS
Nogales, E	1999	96	79	Cell	HCAPLUS
Nogales, E	1998	391	199	Nature	HCAPLUS
Oakley, B	1994		33	no publication given	HCAPLUS
Owellen, R	1972	47	685	Biochem Biophys Res	HCAPLUS
Pettit, G	1993	58	1302	J Org Chem	HCAPLUS
Prade, L	1997	5	1627	Structure	HCAPLUS
Ranganathan, S	1998	77	562	Br J Cancer	HCAPLUS
Rawlings, D	1994	138	105	Immunol Rev	HCAPLUS
Rawlings, D	1993	261	358	Science	HCAPLUS
Remillard, S	1975	189	1002	Science	HCAPLUS
Schiff, P	1979	277	665	Nature	HCAPLUS
Schwartz, G	1997	3	537	Clin Cancer Res	HCAPLUS
Shi, Q	1998	4	219	Curr Pharm Des	HCAPLUS
Shtil, A	1999	18	377	Oncogene	HCAPLUS
Sicheri, F	1997	385	602	Nature	HCAPLUS
Siemasko, K	1998	160	1581	J Immunol	HCAPLUS
Srivastava, R	1999	96	3775	Proc Natl Acad Sci U	HCAPLUS
Sudbeck, E	1999	5	1569	Clin Can Res	HCAPLUS
Takahashi, M	1987	40	66	J Antibiot (Tokyo)	HCAPLUS
Takahashi, T	1994	342	124	FEBS Lett	HCAPLUS
Takemoto, S	1997	94	13897	Proc Natl Acad Sci U	HCAPLUS
Tapley, P	1992	7	371	Oncogene	HCAPLUS
Teicher, B	1999	39	313	Adv Enzyme Regul	HCAPLUS
Ter Haar, E	1996	35	243	Biochemistry	HCAPLUS
Thavasu, P	1999	59	3980	Cancer Res	HCAPLUS
Toi, M	1991	27	977	European J Cancer	MEDLINE
Tortolani, P	1995	155	5220	J Immunol	HCAPLUS
Traxler, P	1997	40	3601	J Med Chem	HCAPLUS
Tsukada, S	1993	72	279	Cell	HCAPLUS
Uckun, F	1998	56	683	Biochemical Pharmaco	HCAPLUS
Uckun, F	2000	10	1015	Bioorg Med Chem Lett	HCAPLUS
Uckun, F	2000	10	541	Bioorg Med Chem Lett	HCAPLUS
Uckun, F	1995	85	2817	Blood	HCAPLUS
Uckun, F	1998	4	1125	Clin Cancer Res	HCAPLUS
Uckun, F	1998	4	901	Clinical Cancer Rese	HCAPLUS
Uckun, F	1995	267	886	Science	MEDLINE
Uckun, F	1996	273	1096	Science	HCAPLUS
Vassilev, A	1999	274	1646	J Biol Chem	HCAPLUS
Vetrie, D	1993	361	226	Nature	HCAPLUS
Vihinen, M	1995	16	460	Immunol Today	HCAPLUS
Wallin, M	1985	179	289	FEBS Lett	HCAPLUS
Wang, L	1999	162	3897	J Immunol	HCAPLUS
Wang, T	1998	273	4928	J Biol Chem	HCAPLUS
Wasik, M	1998	28	551	Leuk Lymphoma	HCAPLUS
Wesselborg, S	1999	93	3053	Blood	HCAPLUS
Wilks, A	1991	11	2057	Mol Cell Biol	HCAPLUS

Witthuhn, B	1999	32	289	Leukemia and Lymphom	HCAPLUS
Xu, X	1996	52	527	Biochem Pharmacol	HCAPLUS
Yamamoto, K	1999	19	8469	Mol Cell Biol	HCAPLUS
Yamashita, N	1997	50	440	J Antibiot (Tokyo)	HCAPLUS
Zaman, G	1999	57	57	Biochem Pharmacol	HCAPLUS
Zhang, Q	1996	93	9148	Proc Natl Acad Sci U	HCAPLUS

L58 ANSWER 10 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:411480 HCAPLUS
DN 135:221035
TI Role of a **JAK3**-dependent biochemical signaling pathway in platelet activation and aggregation
AU Tibbles, Heather E.; Vassilev, Alexei; Wendorf, Heather; Schonhoff, Dawn; Zhu, Dan; Lorenz, David; Waurzyniak, Barbara; Liu, Xing-Ping; **Uckun, Fatih M.**
CS Parker **Hughes** Cancer Center, the Departments of Hematology, Biochemistry, Parker **Hughes Institute**, St. Paul, MN, 55113, USA
SO Journal of Biological Chemistry (2001), 276(21), 17815-17822
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Here we provide exptl. evidence that identifies **JAK3** as one of the regulators of platelet function. Treatment of platelets with thrombin induced tyrosine phosphorylation of the **JAK3** target substrates STAT1 and STAT3. Platelets from **JAK3**-deficient mice displayed a decrease in tyrosine phosphorylation of STAT1 and STAT3. In accordance with these data, pretreatment of human platelets with the **JAK3** inhibitor **WHI-P131** markedly decreased the base-line enzymic activity of constitutively active **JAK3** and abolished the thrombin-induced tyrosine phosphorylation of STAT1 and STAT3. Following thrombin stimulation, **WHI-P131**-treated platelets did not undergo shape changes indicative of activation such as pseudopod formation. **WHI-P131** inhibited thrombin-induced degranulation/serotonin release as well as platelet aggregation. Highly effective platelet inhibitory plasma concns. of **WHI-P131** were achieved in mice without toxicity. **WHI-P131** prolonged the bleeding time of mice in a dose-dependent manner and improved event-free survival in a mouse model of thromboplastin-induced generalized and invariably fatal thromboembolism. To our knowledge, **WHI-P131** is the first antithrombotic agent that prevents platelet aggregation by inhibiting **JAK3**.
IT **202475-60-3**, **WHI-P131**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(role of a **JAK3**-dependent biochem. signaling pathway in platelet activation and aggregation)
RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **157482-36-5, JAK3 kinase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(role of a **JAK3**-dependent biochem. signaling pathway in platelet activation and aggregation)
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Asselin, J	1997	89	1235	Blood	HCAPLUS
D'Cruz, O	1998	59	503	Biol Reprod	HCAPLUS
Ezumi, Y	1998	188	267	J Exp Med	HCAPLUS
Goodman, P	1998	273	17742	J Biol Chem	HCAPLUS
Hammes, S	1999	38	2486	Biochemistry	HCAPLUS
Hirao, A	1997	16	2342	EMBO J	HCAPLUS
Imada, K	2000	37	1	Mol Immunol	HCAPLUS
Kahn, M	1999	103	879	J Clin Invest	HCAPLUS
Laffargue, M	1999	443	66	FEBS Lett	HCAPLUS
Mahajan, S	1999	274	9587	J Biol Chem	HCAPLUS
Mahajan, S	1995	15	5304	Mol Cell Biol	HCAPLUS
Melford, S	1997	272	27539	J Biol Chem	HCAPLUS
Nosaka, T	1995	270	800	Science	HCAPLUS
Oda, A	1992	267	20075	J Biol Chem	HCAPLUS
Pasquet, J	2000	275	28526	J Biol Chem	HCAPLUS
Quek, L	1998	8	1137	Curr Biol	HCAPLUS
Rodriguez-Linares, B	1994	352	335	FEBS Lett	HCAPLUS
Sada, K	1997	248	827	Eur J Biochem	HCAPLUS
Sato, K	1998	78	191	Jpn J Pharmacol	HCAPLUS
Sudbeck, E	1999	5	1569	Clin Cancer Res	HCAPLUS
Teng, C	1997	320	161	Eur J Pharmacol	HCAPLUS
Tohyama, Y	1994	269	32796	J Biol Chem	HCAPLUS
Treco, D	1995	1	2.1.1	Current Protocols in	
Uckun, F	1996	271	6389	J Biol Chem	HCAPLUS
Uckun, F	1996	273	1096	Science	HCAPLUS
Vassilev, A	1999	274	1646	J Biol Chem	HCAPLUS
White, J	1983		1	Methods in Hematolog	
Witthuhn, B	1999	32	289	Leuk Lymphoma	HCAPLUS

L58 ANSWER 11 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:380561 HCAPLUS
DN 134:366897
TI Preparation and pharmaceutical use of **4-(4'-hydroxyphenyl)amino-6,7-**

dimethoxyquinazoline to prevent the development of colorectal cancer

IN **Uckun, Fatih M.**

PA Parker **Hughes Institute**, USA

SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001036394	A1	20010525	WO 2000-US31188	20001114
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1232146	A1	20020821	EP 2000-977201	20001114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003514803	T2	20030422	JP 2001-538883	20001114
US 6482828	B1	20021119	US 2002-145639	20020514
US 2002183340	A1	20021205		
PRAI US 1999-165499P	P	19991115		
WO 2000-US31188	W	20001114		

AB Preventing the development or recurrence of colorectal cancer in a mammal comprising administering an effective cancer-preventive amount of **4**-(**4'-hydroxyphenyl**)-**amino-6**,**7-dimethoxyquinazoline** (m.p. 245.0-248.0°; prepared in seven steps from 3,4-dimethoxy-6-nitrobenzoic acid) or a pharmaceutically acceptable salt.

IT **340176-69-4P 340176-70-7P 340176-72-9P**
340176-73-0P 340176-75-2P 340176-77-4P
340176-81-0P 340176-82-1P 340176-83-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and pharmaceutical use of **4**-(**4'-hydroxyphenyl**)**amino-6**,**7-dimethoxyquinazoline** and its salts to prevent the development of colorectal cancer)

RN 340176-69-4 HCAPLUS

CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]-, 4-methylbenzenesulfonate (salt) (9CI) (CA INDEX NAME)

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CRN 202475-60-3
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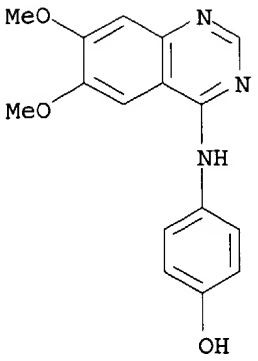

CM 2

CRN 104-15-4
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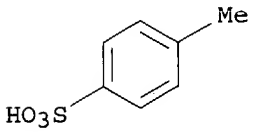

RN 340176-70-7 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]-, methanesulfonate (salt) (9CI) (CA INDEX NAME)

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CRN 202475-60-3
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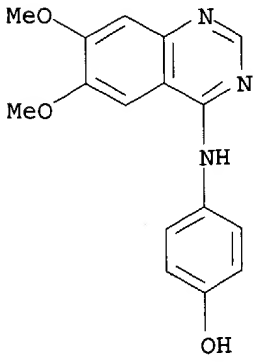

CM 2

CRN 75-75-2
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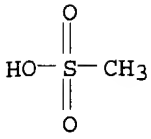

RN 340176-72-9 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]-, acetate (salt) (9CI) (CA INDEX NAME)

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CRN 202475-60-3
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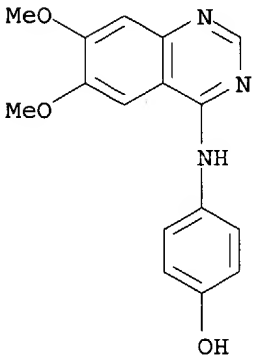

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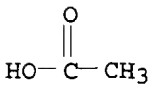

RN 340176-73-0 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]-, 2-hydroxy-1,2,3-propanetricarboxylate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 202475-60-3
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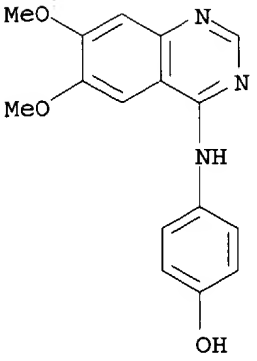

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CRN 77-92-9
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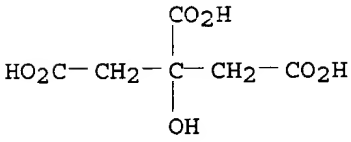
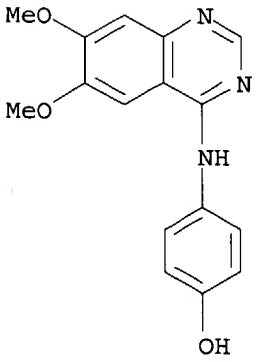


RN 340176-75-2 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]-, (2R,3R)-2,3-dihydroxybutanedioate (salt) (9CI) (CA INDEX NAME)

CM 1

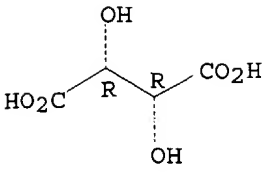
CRN 202475-60-3
CMF C16 H15 N3 O3



CM 2

CRN 87-69-4
CMF C4 H6 O6

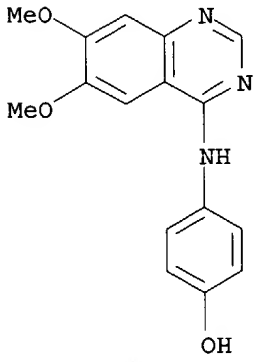
Absolute stereochemistry.



RN 340176-77-4 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]-, benzoate (salt) (9CI) (CA INDEX NAME)

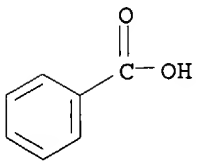
CM 1

CRN 202475-60-3
CMF C16 H15 N3 O3



CM 2

CRN 65-85-0
CMF C7 H6 O2



RN 340176-81-0 HCAPLUS
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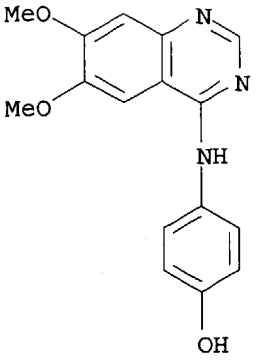

● x HCl

RN 340176-82-1 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]-, sulfate (salt) (9CI) (CA INDEX NAME)

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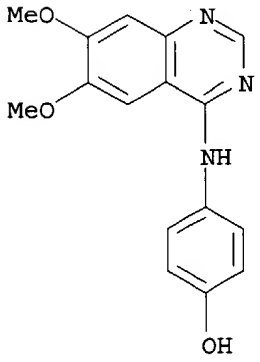
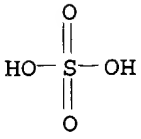
CRN 202475-60-3
CMF C16 H15 N3 O3



CM 2

CRN 7664-93-9
CMF H2 O4 S



RN 340176-83-2 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]-, nitrate (salt) (9CI) (CA INDEX NAME)

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CRN 202475-60-3
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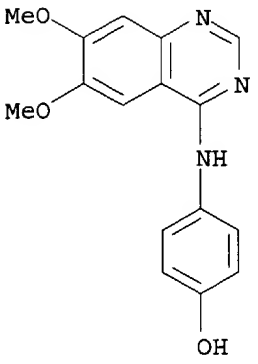

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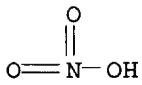
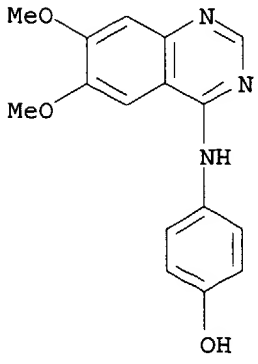


IT **202475-60-3P, 4-(4'-Hydroxyphenyl) amino-6,7-dimethoxyquinazoline**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and pharmaceutical use of **4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline** to prevent the development of colorectal cancer)
RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RETABLE

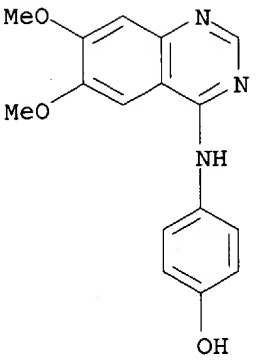
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Goodman, P	1998	273	17742	JOURNAL OF BIOLOGICA	HCAPLUS
Myers, M	1998			US 5721237 A	HCAPLUS
Parker Hughes Instit	2000			WO 0056720 A	HCAPLUS
Rama, K	1998	4	2463	CLINICAL CANCER RESE	
Uckun, F	1999	5	2954	CLINICAL CANCER RESE	HCAPLUS
Wayne Hughes Instit	1999			WO 9961428 A	HCAPLUS

L58 ANSWER 12 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:380393 HCAPLUS
DN 134:363426
TI Radiosensitization of human glioblastoma cells by quinazoline compounds
IN **Uckun, Fatih M.**; Narla, Rama K.
PA Parker **Hughes Institute**, USA
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

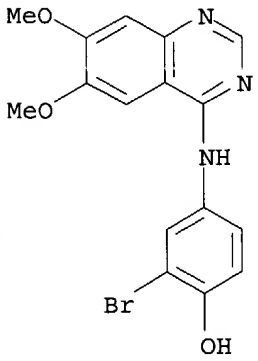
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001035952	A2	20010525	WO 2000-US31287	20001114

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-165488P P 19991115
OS MARPAT 134:363426
AB The present invention is directed to a method of sensitizing cancer cells to radiation treatment by subjecting the cells to suitable quinazoline derivs., such as **4-(3'-bromo-4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline**, or its pharmaceutically acceptable salt. The present invention is further directed to a cancer treatment, which includes a combination of (a) radiation and (b) a radiation-sensitizing amount of a suitable quinazoline derivs. or its pharmaceutically acceptable salt.
IT **202475-60-3P**, **WHI-P131 211555-04-3P**, **WHI-P154**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(radiosensitization of human glioblastoma cells by quinazoline compds.)
RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 211555-04-3 HCAPLUS
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



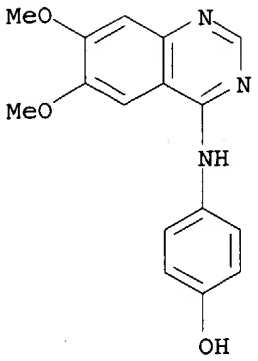
L58 ANSWER 13 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:42652 HCAPLUS
DN 134:155488
TI 4-[(3-Bromo-4-hydroxyphenyl)amino]-6,7-dimethoxyquinazolin-1-ium chloride methanol solvate and 4-[(3-hydroxyphenyl)amino]-6,7-dimethoxy-1-quinazolinium chloride
AU Ghosh, Sutapa; Jennissen, Jason D.; Liu, Xing Ping; **Uckun, Fatih M.**
CS Department of Structural Biology, Parker **Hughes Institute**, St Paul, MN, 55113, USA
SO Acta Crystallographica, Section C: Crystal Structure Communications (2001), C57(1), 76-78
CODEN: ACSCEE; ISSN: 0108-2701
PB Munksgaard International Publishers Ltd.
DT Journal
LA English
AB The title compds., C16H15BrN3O3+·Cl-·CH4O (**WHI-P154**) and C16H16N3O3+·Cl- (WHI-P180), are potent inhibitors [**WHI-P154** with IC50 = 5.6 μM and WHI-P180 with IC50 = 4.0 μM for epidermal growth factor receptor (EGFR) kinase inhibition] of the EGFR tyrosine kinase as well as **Janus Kinase 3**. The mol. structures of these compds. are very similar except for the dihedral angle between the anilino and quinazoline moieties which is 1.10(5)° for **WHI-P154**, and 45.66(6) and 25.29(7)° for the two mols. of WHI-P180 in the asym. unit. The N at the N3 position is protonated in both structures and participates in H

bonding with the Cl anions. Crystallog. data are given.

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Bruker	1998			SMART, SAINT and SHE	
Ghosh, S	1999	14	403	Anti-Cancer Drug Des	HCAPLUS
Ghosh, S	1998	4	2657	Clin Cancer Res	HCAPLUS
Narla, R	1998	4	1405	Clin Cancer Res	HCAPLUS
Sheldrick, G	1990	A46	467	Acta Cryst	HCAPLUS
Sheldrick, G	1996			SADABS	
Sheldrick, G	1997			SHELXL97	
Sudbeck, E	1999	5	1569	Clin Cancer Res	HCAPLUS

L58 ANSWER 14 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:846101 HCAPLUS
DN 134:141589
TI Treatment of allergic asthma by targeting **Janus kinase 3**-dependent leukotriene synthesis in mast cells with 4-(3',5'-dibromo-4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline (WHI-P97)
AU Malaviya, Ravi; Chen, Chun-Lin; Navara, Christopher; Malaviya, Rama; Liu, Xing-Ping; Keenan, Margaret; Waurzyniak, Barbara; **Uckun, Fatih M.**
CS Departments of Allergy and Inflammatory Diseases, Parker **Hughes Institute**, St. Paul, MN, USA
SO Journal of Pharmacology and Experimental Therapeutics (2000), 295(3), 912-926
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB 4-(3',5'-Dibromo-4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline (WHI-P97) is a rationally designed potent inhibitor of Janus kinase (**JAK**)-**3**. Treatment of mast cells with WHI-P97 inhibited the translocation of 5-lipoxygenase (5-LO) from the nucleoplasm to the nuclear membrane and consequently 5-LO-dependent leukotriene (LT) synthesis after IgE receptor/FcεRI crosslinking by >90% at low micromolar concns. WHI-P97 did not directly inhibit the enzymic activity of 5-LO, but prevented its translocation to the nuclear membrane without affecting the requisite calcium signal. WHI-P97 was very well tolerated in mice, with no signs of toxicity at dose levels ranging from 5 μg/kg to 50 mg/kg, and LD10 was not reached at a 50 mg/kg dose level when administered as a single i.p. or i.v. bolus dose. Therapeutic WHI-P97 concns., which inhibit mast cell leukotriene synthesis in vitro, could easily be achieved in vivo after the i.v. or i.p. administration of a single nontoxic 40 mg/kg bolus dose of WHI-P97. Notably, WHI-P97 showed promising biol. activity in a mouse model of allergic asthma at nontoxic dose levels. Treatment of ovalbumin-sensitized mice with WHI-P97 prevented the development of airway hyper-responsiveness to methacholine in a dose-dependent fashion. Furthermore, WHI-P97 inhibited the eosinophil recruitment to the airway lumen after the ovalbumin challenge in a dose-dependent fashion. Further development of WHI-P97 may therefore provide the basis for new and effective treatment as well as prevention programs for allergic asthma in clin. settings.
IT **202475-60-3**, **WHI-P131**
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(treatment of allergic asthma by targeting **Janus kinase 3**-dependent leukotriene synthesis in mast cells with quinazoline WHI-P97)
RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **157482-36-5, Janus kinase 3**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(treatment of allergic asthma by targeting **Janus kinase 3**-dependent leukotriene synthesis in mast cells with quinazoline WHI-P97)
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Abramovitz, M	1993	215	105	Eur J Biochem	HCAPLUS
An, S	1998	1		Allergy, Principles	
Arm, J	1992	51	323	Adv Immunol	HCAPLUS
Brock, T	1995	23	151	Adv Prostaglandin Th	HCAPLUS
Brock, T	1998	329	519	Biochem J	HCAPLUS
Brock, T	1994	269	22059	J Biol Chem	HCAPLUS
Buendia, B	1999	112	1743	J Cell Sci	HCAPLUS
Chen, C	1999	724	157	J Chromatogr B Biome	HCAPLUS
Chen, C	1999	727	205	J Chromatogr B Biome	HCAPLUS
Chen, C	1999	16	1003	Pharm Res (NY)	HCAPLUS
Chen, C	1999	16	117	Pharm Res (NY)	HCAPLUS
Coffey, M	1994	11	153	Am J Respir Cell Mol	HCAPLUS
Costello, P	1996	13	2595	Oncogene	HCAPLUS
Dahlen, S	1983	80	1712	Proc Natl Acad Sci U	HCAPLUS
Davies, B	1993	10	1093	Pharm Res (NY)	MEDLINE
Drazen, J	1999	340	197	N Engl J Med	MEDLINE
Drazen, J	1980	77	4354	Proc Natl Acad Sci U	HCAPLUS
Galli, S	1993	328	257	N Engl J Med	MEDLINE
Gorenne, I	1994	268	868	J Pharmacol Exp Ther	HCAPLUS
Hamawy, M	1997	201	11	J Immunol Methods	HCAPLUS
Hamelmann, E	1997	16	674	Am J Respir Cell Mol	MEDLINE
Hamelmann, E	1997	156	766	Am J Respir Crit Car	MEDLINE
Hamelmann, E	1997	155	819	Am J Respir Crit Car	MEDLINE
Hamelmann, E	1997	94	1350	Proc Natl Acad Sci U	HCAPLUS
Henderson, W	1996	184	1483	J Exp Med	HCAPLUS
Hirasawa, N	1995	154	5391	J Immunol	HCAPLUS
Ihle, J	1995	13	369	Annu Rev Immunol	HCAPLUS
Ihle, J	1995	11	69	Trends Genet	HCAPLUS
Ishizaka, T	1971	106	1267	J Immunol	HCAPLUS
Jakschik, B	1980	287	51	Nature (Lond)	HCAPLUS
Laemmli, U	1970	227	680	Nature (Lond)	HCAPLUS
Laitinen, L	1993	341	989	Lancet	MEDLINE
Lee, J	1997	185	2143	J Exp Med	HCAPLUS

Leng, W	1988	140	2361	J Immunol	HCAPLUS
Lepley, R	1996	271	6179	J Biol Chem	HCAPLUS
Liu, F	1980	124	2728	J Immunol	HCAPLUS
Malaviya, R	1999	257	807	Biochem Biophys Res	HCAPLUS
Malaviya, R	1993	268	4939	J Biol Chem	HCAPLUS
Malaviya, R	1999	274	27028	J Biol Chem	HCAPLUS
Malaviya, R	1995	253	27	Methods Enzymol	MEDLINE
Messinger, Y	1998	4	165	Clin Cancer Res	HCAPLUS
Negri, C	1992	200	452	Exp Cell Res	HCAPLUS
Peters-Golden, M	1998	157	S227	Am J Respir Crit Car	MEDLINE
Ramos, B	1992	262	559	J Pharmacol Exp Ther	HCAPLUS
Smith, L	1996	156	2181	Arch Intern Med	HCAPLUS
Sohn, S	1998	160	2130	J Immunol	HCAPLUS
Sorkness, C	1997	17	50S	Pharmacotherapy	HCAPLUS
Spada, C	1997	400B	699	Adv Exp Med Biol	HCAPLUS
Spada, C	1994	55	183	J Leukoc Biol	HCAPLUS
Sudbeck, E	1999	5	1569	Clin Cancer Res	HCAPLUS
Takeda, K	1997	186	449	J Exp Med	HCAPLUS
Tan, R	1998	4	25	Curr Opin Pulm Med	MEDLINE
Uckun, F	1992	79	2649	Blood	HCAPLUS
Uckun, F	1993	81	3052	Blood	MEDLINE
Uckun, F	1998	4	1125	Clin Cancer Res	HCAPLUS
Wasserman, S	1994	150	S39	Am J Respir Crit Car	MEDLINE
Wasserman, S	1990	86	590	J Allergy Clin Immun	MEDLINE
Wei, Y	1986	137	1993	J Immunol	HCAPLUS
Wong, A	1992	31	4046	Biochemistry	HCAPLUS
Xu, L	1993	45	385	Prostaglandins	HCAPLUS
Zhang, Y	1992	258	1957	Science (Wash DC)	HCAPLUS
Zini, N	1994	210	336	Exp Cell Res	HCAPLUS

L58 ANSWER 15 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:787792 HCAPLUS
DN 133:327883
TI An inhibitor of **janus kinase 3**: 4-(4-hydroxyphenylamino)-6,7-dimethoxyquinazolin-1-ium chloride methanol solvate
AU Sudbeck, Elise A.; Jennissen, Jason D.; Liu, Xing-Ping; **Uckun, Fatih M.**
CS Drug Discovery Program, Department of Structural Biology, Parker **Hughes Institute**, St Paul, MN, USA
SO Acta Crystallographica, Section C: Crystal Structure Communications (2000), C56(10), 1282-1283
CODEN: ACSCEE; ISSN: 0108-2701
PB Munksgaard International Publishers Ltd.
DT Journal
LA English
AB The crystal structure of the title compound, C16H16N3O3+·Cl-·CH4O (**WHI-P131**, an inhibitor of **Janus kinase 3**), contains four H bonds. There are two H bonds within the asym. unit, i.e. interactions between **WHI-P131** OH and Cl-, and between MeOH and Cl-. There is a 3rd interaction between **WHI-P131** NH and Cl- (related by a 21 screw) and a 4th between **WHI-P131** NH and MeOH (related by an n-glide). The H-bond pattern for these interactions can be described by the 1st-level H-bond graph-set notation D11(2)D11(2)D11(2)D11(2). The 2nd-level graph-set notation (for combinations of two H bonds) is D21(3)D21(3)D22(4)D22(9)D22(14)C21(9). Crystallog. data are given.

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Bernstein, J	1995	34	1555	Angew Chem Int Ed En	HCAPLUS

Bernstein, J	1990		695	J Chem Soc Perkin Tr	HCAPLUS
Bruker	1998			SAINT, SMART and SHE	
Etter, M	1990	23	120	Acc Chem Res	HCAPLUS
Etter, M	1990	B46	256	Acta Cryst	HCAPLUS
Etter, M	1991	95	4601	J Phys Chem	HCAPLUS
Malaviya, R	1999	274	27028	J Biol Chem	HCAPLUS
Sheldrick, G	1996			SADABS	
Sheldrick, G	1997			SHELXS97 and SHELXL9	
Sudbeck, E	1999	5	1569	Clin Cancer Res	HCAPLUS

L58 ANSWER 16 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:688226 HCAPLUS
DN 133:266866
TI Preparation of quinazolines as antitumor agents
IN **Uckun, Fatih M.**; Liu, Xing-ping; Narla, Rama K.
PA Parker **Hughes Institute**, USA
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000056720	A1	20000928	WO 2000-US6902	20000316
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6258820	B1	20010710	US 1999-357404	19990720
	EP 1163228	A1	20011219	EP 2000-921389	20000316
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002540103	T2	20021126	JP 2000-606581	20000316
	US 2001016588	A1	20010823	US 2001-779809	20010208
	US 6358962	B2	20020319		
	US 2002137757	A1	20020926	US 2001-923903	20010807
	US 6638939	B2	20031028		
	NO 2001004560	A	20010919	NO 2001-4560	20010919
	US 2004039002	A1	20040226	US 2003-454960	20030605
PRAI	US 1999-125145P	P	19990319		
	US 1999-125177P	P	19990319		
	US 1999-125338P	P	19990319		
	US 1999-357404	A	19990720		
	WO 2000-US6902	W	20000316		
	US 2001-779809	A1	20010208		
	US 2001-923903	A1	20010807		

OS MARPAT 133:266866
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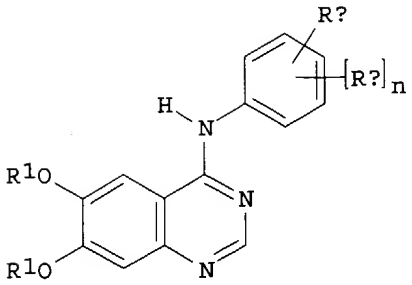


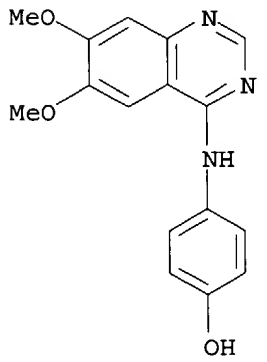
I

AB The title compds. [I; Ra = I, hydroxyalkyl, methylenedioxy, etc.; n = 1-4; Rb = H, halo, OH, etc.; R1 = alkyl], useful for the treatment of cancer (e.g., leukemia and breast cancer) and for the treatment of allergic reactions, were prepared by reacting 4-chloro-6,7-dimethoxyquinazoline with the substituted aniline. Biol. data for compds. I were given.

IT **188829-39-2P 202475-60-3P 211555-04-3P**
296234-84-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazolines as antitumor agents)

RN 188829-39-2 HCAPLUS

CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]-, monohydrochloride (9CI) (CA INDEX NAME)



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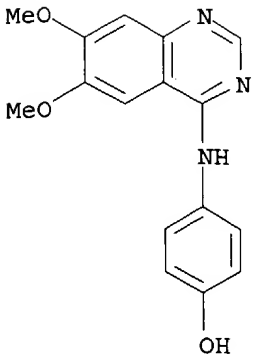
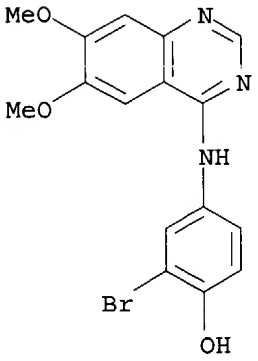
RN 202475-60-3 HCAPLUS

CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 211555-04-3 HCAPLUS
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 296234-84-9 HCAPLUS
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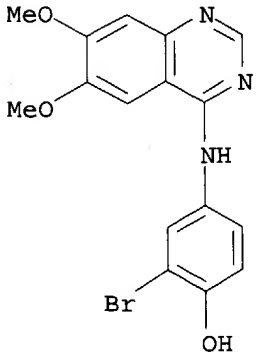

● HCl

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File

Narla	1998	4	1405	CLINICAL CANCER RESE	HCAPLUS
Rhone Poulenc	1995			WO 9515758 A	HCAPLUS
Rhone Poulenc	1998			US 5721237 A	HCAPLUS
Sugen	1995			WO 9521613 A	HCAPLUS
Sugen	1998			WO 9810767 A	HCAPLUS
Wayne, H	1999			WO 9961428 A	HCAPLUS
Wellcome	1996			WO 9609294 A	HCAPLUS
Zeneca	1993			EP 0566226 A	HCAPLUS
Zeneca	1995			US 5457105 A	HCAPLUS
Zeneca	1997			WO 9732856 A	HCAPLUS

L58 ANSWER 17 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:688094 HCAPLUS
DN 133:271682
TI Preparation of quinazolines for micellar pharmaceuticals for treatment of allergy and cancer
IN Yiv, Seang; Li, Mingshu; **Uckun, Fatih M.**
PA Parker **Hughes Institute**, USA
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000056338	A1	20000928	WO 2000-US7066	20000317
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1162974	A1	20011219	EP 2000-914991	20000317
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	JP 2002539262	T2	20021119	JP 2000-606242	20000317
	US 2002111360	A1	20020815	US 2001-960464	20010919
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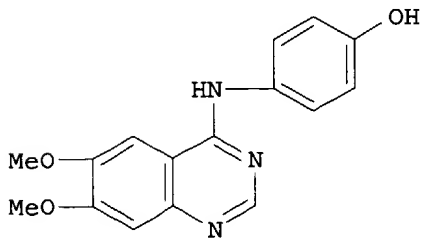
	WO 2000-US7066	W	20000317		

OS MARPAT 133:271682
GI



I

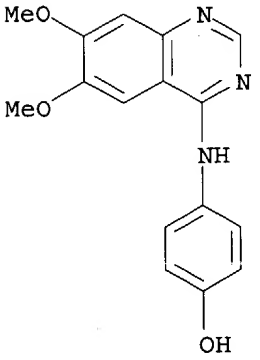
AB Pharmaceutical compns. for parenteral administration of poorly soluble quinazoline compds. in the form of microemulsions or micellar solns. are described. The compns. are useful in treating patients suffering from

cancer or having allergic reactions. E.g., I was prepared, its soly profile given, and micellar solns. containing PEGylated phosphatidylethanolamines were effective in enhancing the solubilization of I.

IT **202475-60-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation of quinazolines for micellar pharmaceuticals for treatment of allergy and cancer)

RN 202475-60-3 HCAPLUS

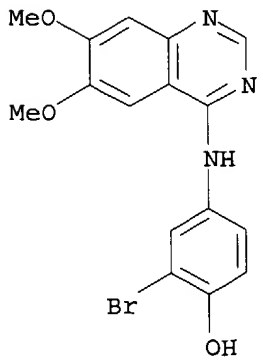
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **211555-04-3P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazolines for micellar pharmaceuticals for treatment of allergy and cancer)

RN 211555-04-3 HCAPLUS

CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Brassinne, C	1983	70	1081	JOURNAL OF THE NATIO	HCAPLUS
Davidson, C	1996			WO 9606616 A	HCAPLUS
Dreikorn, B	1995			US 5411963 A	HCAPLUS
Gazit, A	1998			US 5792771 A	HCAPLUS
Imarx Pharmaceutical Co	1998			WO 9851284 A	HCAPLUS

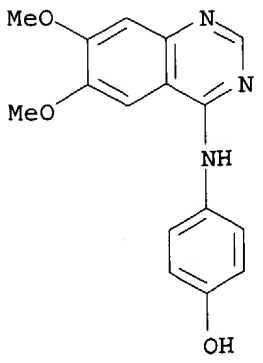
Scwinn, J	1998	232	35	JOURNAL OF RADIOANAL	
Slavin, S	1995			US 5449678 A	HCAPLUS
Sugen Inc	1998			WO 9838984 A	HCAPLUS
Troponwerke Gmbh & Co K	1983			EP 0082385 A	HCAPLUS
Yiv, S	1999	217	148	ABSTRACTS OF PAPERS	

L58 ANSWER 18 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:627969 HCAPLUS
DN 133:187943
TI Hydroxyhaloquinazolines for augmentation of mast cell bactericidal activity
IN **Uckun, Fatih M.**; Malaviya, Ravi
PA Parker **Hughes Institute**, USA
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

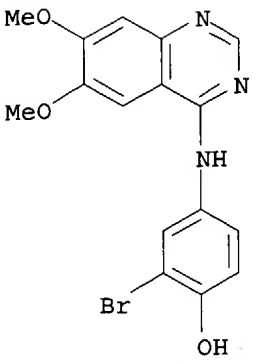
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000051581	A2	20000908	WO 2000-US3825	20000215
	WO 2000051581	A3	20010405		

W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-264141 A 19990305
AB Hydroxyhaloquinazolines are provided for the augmentation of mast cell anti-microbial activity.
IT **202475-60-3P**, **WHI-P131 211555-04-3P**, **WHI-P154**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(hydroxyhaloquinazolines for augmentation of mast cell antimicrobial activity)
RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 211555-04-3 HCAPLUS
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L58 ANSWER 19 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:433345 HCAPLUS
DN 133:53698
TI **JAK-3** inhibitors for treating allergic disorders
IN **Uckun, Fatih M.**; Malavia, Ravi; Sudbeck, Elise A.
PA **Hughes Institute, USA**
SO U.S., 42 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6080747	A	20000627	US 1999-263420	19990305
	US 6080748	A	20000627	US 1999-361491	19990726
	US 6177433	B1	20010123	US 1999-443847	19991119
	WO 2000051587	A2	20000908	WO 2000-US5353	20000301
	WO 2000051587	A3	20001221		
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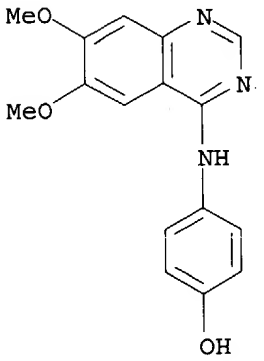
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1158968	A2	20011205	EP 2000-913691	20000301
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002538107	T2	20021112	JP 2000-602055	20000301
	US 6313130	B1	20011106	US 2000-627342	20000728
	US 6326373	B1	20011204	US 2000-688755	20001016
	US 2002055514	A1	20020509	US 2001-791040	20010222
	US 6452005	B1	20020917		
	NO 2001004303	A	20010904	NO 2001-4303	20010904
	US 2002165243	A1	20021107	US 2002-128683	20020423
PRAI	US 1999-263420	A1	19990305		
	US 1999-443847	A1	19991119		
	WO 2000-US5353	W	20000301		
	US 2000-627342	A1	20000728		
	US 2001-791040	A1	20010222		

OS MARPAT 133:53698
AB Inhibitors of **JAK-3 kinase** for the treatment of allergy inhibit mast cell degranulation and mediator release.

Quinazoline derivs. were prepared as **JAK-3 kinase** inhibitors.

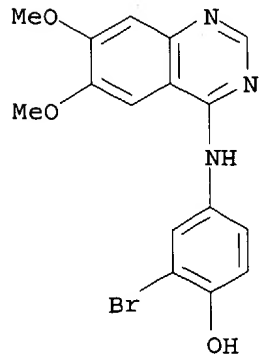
IT **202475-60-3P, WHI-P131**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation of quinazoline derivs. as **JAK-3** inhibitors for treating allergic disorders in relation to inhibition of mast cell degranulation and pharmacokinetics and toxicity)

RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **211555-04-3P, WHI-P154**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation of quinazoline derivs. as **JAK-3** inhibitors for treating allergic disorders in relation to inhibition of mast cell degranulation and pharmacokinetics and toxicity)

RN 211555-04-3 HCAPLUS
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **157482-36-5, JAK3 kinase**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(preparation of quinazoline derivs. as **JAK-3** inhibitors for treating allergic disorders in relation to inhibition of mast cell

degranulation and pharmacokinetics and toxicity)
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Amir, S	1991	203	125	Eur J Pharmaocl	HCAPLUS
Apgar, J	1997	110	771	J Cell Sci	HCAPLUS
Blank, U	1989	337	187	Nature	HCAPLUS
Bohm, H	1994	8	243	J Comput Aided Mol D	MEDLINE
Borch	1990			US 4938949	HCAPLUS
Buckley, R	1997	130	378	J Pediatr	MEDLINE
Chen, C	1999	16	117	Pharmaceutical Resea	HCAPLUS
Clemence	1998			US 5817674	HCAPLUS
Costello, P	1996	13	2595	Oncogene	HCAPLUS
Danial, N	1995	269	1875	Science	HCAPLUS
Darnell, J	1994	264	1415	Science	HCAPLUS
Deckert, M	1998	273	8867	J Biol Chem	HCAPLUS
Dvorak, A	1994	144	160	Am J Pathol	HCAPLUS
Endo, T	1997	387	921	Nature	HCAPLUS
Fusaki, N	1997	272	6214	J Biol Chem	HCAPLUS
Galli, S	1993	328	257	New Eng J Med	MEDLINE
Geria	1991			US 4992478	HCAPLUS
Ghosh, S	1998	4	2657	Clin Cancer Res	HCAPLUS
Goodman, P	1998	273	17742	J Biol Chem	HCAPLUS
Gordon, J	1990	346	274	Nature	HCAPLUS
Gurniak, C	1996	87	3151	Blood	HCAPLUS
Hamawy, M	1995	7	535	Cellular Signalling	HCAPLUS
Hanissian, S	1997	6	379	Immunity	HCAPLUS
Hirasawa, N	1995	270	10960	J Biol Chem	HCAPLUS
Hoffman, S	1997	43	109	Genomics	HCAPLUS
Hogan, A	1997	13	43	Methods:A Companion	HCAPLUS
Hubbard, S	1994	372	746	Nature	HCAPLUS
Hubbard, S	1997	16	5572	The EMBO Journal	HCAPLUS
Ihle, J	1996	351	159	Phil Trans R Soc Lon	HCAPLUS
Ihle, J	1995	11	69	Trends in Genetics	HCAPLUS
Irani, A	1989	37	1509	J Histochem Cytochem	
Jacquet	1986			US 4608392	HCAPLUS
Johnston, J	1995	270	28527	J Biol Chem	HCAPLUS
Johnston, J	1994	370	151	Nature	HCAPLUS
Kumar, A	1996	13	2009	Oncogene	HCAPLUS
Lavens-Phillips, S	1998	47	137	Inflamm Res	HCAPLUS
Leonard, W	1996	2	968	Nature Medicine	HCAPLUS
Levy, D	1997	8	81	Cytokine & Growth Fa	HCAPLUS
Liu, F	1980	124	2728	J Immunol	HCAPLUS
Mahajan, S	1999	274	9587	J Biol Chem	HCAPLUS
Mahajan, S	1995	15	5304	Mol Cell Biol	HCAPLUS
Malaviya, R	1994	268	4939	J Biol Chem	
Malaviya, R	1994	93	1645	J Clin Invest	MEDLINE
Malaviya, R	1994	152	1907	J Immunol	HCAPLUS
Malaviya, R	1996	106	785	J Invest Dermatol	HCAPLUS
Malaviya, R	1996	381	77	Nature	HCAPLUS
Matsuda, T	1994	83	3457	Blood	HCAPLUS
Millard, P	1989	264	19730	J Biol Chem	HCAPLUS
Miyajima, I	1997	99	901	J Clin Invest	HCAPLUS
Miyazaki, T	1996	27	25	Cancer Surveys, Cell	HCAPLUS
Mohammadi, M	1996	86	577	Cell	HCAPLUS
Mohammadi, M	1997	276	955	Science	HCAPLUS
Moriya, K	1997	94	12539	Proc Natl Acad Sci U	HCAPLUS
Narla, R	1998	4	1405	Clin Cancer Res	HCAPLUS

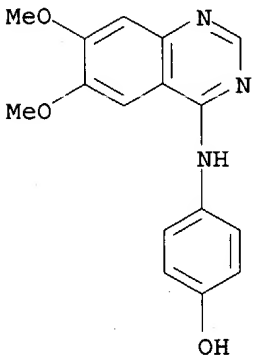
Nelson, B	1996	16	309	Mol Cell Biol	HCAPLUS
Nomoto, Y	1990	38	1591	Chem Pharm Bull	HCAPLUS
Nosaka, T	1995	270	800	Science	HCAPLUS
Oettgen, H	1994	370	367	Nature	HCAPLUS
Oliver, J	1994	269	29697	J Biol Chem	HCAPLUS
Ozawa, K	1993	268	1749	J Biol Chem	HCAPLUS
Reidy, M	1996	37	57	Genomics	
Riske, F	1991	266	11245	J Biol Chem	HCAPLUS
Rolling, C	1996	393	53	FEBS Letters	HCAPLUS
Rolling, C	1995	10	1757	Oncogene	HCAPLUS
Safford, M	1997	25	374	Exp Hematol	HCAPLUS
Safford, M	1997	25	650	Exp Hematol	
Scharenberg, A	1995	61	72	Chem Immunol	HCAPLUS
Scharenberg, A	1995	14	3385	The EMBO Journal	HCAPLUS
Sharfe, N	1997	108	552	Clin Exp Immunol	HCAPLUS
Sicheri, F	1997	385	602	Nature	HCAPLUS
Smith	1985			US 4559157	HCAPLUS
Thomis, D	1997	9	541	Curr Opin Immunol	HCAPLUS
Thomis, D	1995	270	794	Science	HCAPLUS
Tortolani, P	1995	155	5220	J Immunol	HCAPLUS
Uckun, F	1998	4	901	Clin Cancer Res	HCAPLUS
Uckun, F	1996	271	6389	J Biol Chem	HCAPLUS
Uckun, F	1995	267	886	Science	MEDLINE
Uckun, F	1996	273	1096	Science	HCAPLUS
Vassilev, A	1999	274	1646	J Biol Chem	HCAPLUS
Vebrbsky, J	1996	271	13976	J Biol Chem	
Villa, A	1996	88	817	Blood	HCAPLUS
Wei, Y	1986	137	1993	J Immunol	HCAPLUS
Wong, A	1992	31	4046	Biochemistry	HCAPLUS
Wortzman	1989			US 4820508	HCAPLUS
Xia, H	1997	159	2911	J Immunol	HCAPLUS
Yamauchi, T	1998	273	15719	J Biol Chem	HCAPLUS
Yin, T	1995	270	20497	J Biol Chem	HCAPLUS
Zhong, Z	1994	91	4806	Proc Natl Acad Sci U	HCAPLUS
Zhu, D	1998	4	2967	Clin Cancer Res	HCAPLUS

L58 ANSWER 20 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:228537 HCAPLUS
DN 132:342816
TI Structure-based design of potent inhibitors of EGF-receptor tyrosine kinase as anti-cancer agents
AU Ghosh, Sutapa; Narla, Rama Krishna; Zheng, Yaguo; Liu, Xing-Ping; Jun, Xiao; Mao, Chen; Sudbeck, Elise A.; **Uckun, Fatih M.**
CS Parker **Hughes** Cancer Center, Departments of Structural Biology, Parker **Hughes Institute**, St Paul, MN, 55113, USA
SO Anti-Cancer Drug Design (1999), 14(5), 403-410
CODEN: ACDDEA; ISSN: 0266-9536
PB Oxford University Press
DT Journal
LA English
AB In a systematic effort to design inhibitors of the epidermal growth factor receptor (EGFR) family protein tyrosine kinases (PTK) as anti-cancer agents, we have constructed a three-dimensional homol. model of the EGFR kinase domain and used mol. modeling methods for the structure-based design of analogs of the active metabolite of leflunomide (LFM) with potent and specific inhibitory activity against EGFR. These docking studies identified α-cyano-β-hydroxy-β-methyl-N-[4-(trifluoromethoxy)phenyl]-p ropenamide (LFM-A12) as our lead compound, which was predicted to bind to the EGFR catalytic site in a planar conformation. LFM-A12 inhibited the proliferation (IC50 = 26.3 μM) and in vitro invasiveness (IC50=28.4 μM) of EGFR pos. human breast cancer cells in a concentration-dependent fashion. Similarly, the model of the EGFR binding pocket

was used in combination with docking procedures to predict the favorable placement of chemical groups with defined sizes at multiple modification sites on another class of EGFR inhibitors, the 4-anilinoquinazoline. This approach has led to the successful design of a dibromo quinazoline derivative, WHI-P97, which had an estimated Ki value of 0.09 μM from modeling studies and a measured IC50 value of 2.5 μM in EGFR kinase inhibition assays. WHI-P97 effectively inhibited the in vitro invasiveness of EGFR-pos. human cancer cells in a concentration-dependent manner. However, unlike LFM-A12, the quinazoline compds. are not specific for EGFR.

IT **202475-60-3, WHI-P131 211555-04-3, WHI-P154**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structure-based design of potent inhibitors of EGF-receptor tyrosine kinase as anti-cancer agents)

RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 211555-04-3 HCAPLUS
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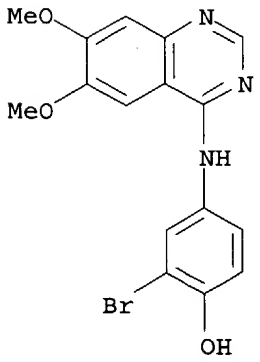

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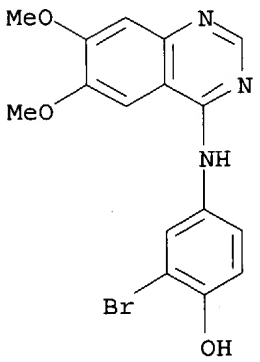
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Bohm, H	1992	6	593	Journal of Computer	MEDLINE
Bohm, H	1994	8	243	Journal of Computer	MEDLINE
Bridges, A	1996	39	267	Journal of Medicinal	HCAPLUS
Carpenter, G	1990	265	7709	Journal of Biologica	HCAPLUS

Chrysogelos, S	1994	29	29	Breast Cancer Resear	MEDLINE
Connolly, M	1983	221	709	Science	HCAPLUS
Earp, H	1995	35	115	Breast Cancer Resear	HCAPLUS
Fox, S	1994	29	41	Breast Cancer Resear	MEDLINE
Fry, D	1995	6	662	Current Opinion in B	HCAPLUS
Fry, D	1994	265	1093	Science	HCAPLUS
George-Nascimento, C	1988	27	797	Biochemistry	HCAPLUS
Ghosh, S	1998	4	2657	Clinical Cancer Rese	HCAPLUS
Hubbard, S	1997	16	5572	EMBO Journal	HCAPLUS
Khazaie, K	1993	12	255	Cancer and Metasis R	HCAPLUS
Mahajan, S	1999	274	9587	Journal of Biologica	HCAPLUS
Mendelsohn, J	1995		607	Biologic Therapy of	
Mohammadi, M	1997	276	955	Science	HCAPLUS
Molecular Simulations	1996			Insight II	
Moyer, J	1997	57	4838	Cancer Research	HCAPLUS
Narla, R	1998	4	1405	Clinical Cancer Rese	HCAPLUS
Palmer, B	1997	40	1519	Journal of Medicinal	HCAPLUS
Rowley, R	1995	270	12659	Journal of Biologica	HCAPLUS
Sicheri, F	1997	385	602	Nature	HCAPLUS
Sudbeck, E	1999	5	1569	Clinical Cancer Rese	HCAPLUS
Toi, M	1991	27	977	European Journal of	MEDLINE
Uckun, F	1998	4	901	Clinical Cancer Rese	HCAPLUS
Wakeling, A	1996	38	67	Breast Cancer Resear	HCAPLUS
Wright, J	1995	270	12085	Journal of Biologica	HCAPLUS
Yarden, Y	1988	57	443	Annual Review of Bio	HCAPLUS
Yoshida, D	1996	39	360	Neurosurgery	MEDLINE
Zheng, J	1993	D49	362	Acta Crystallographi	HCAPLUS
Zhu, D	1998	4	2967	Clinical Cancer Rese	HCAPLUS

L58 ANSWER 21 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:54949 HCAPLUS
DN 132:329420
TI Specificity of α-cyano-β-hydroxy-β-methyl-N-[4-(trifluoromethoxy)phenyl]-p ropenamide as an inhibitor of the epidermal growth factor receptor tyrosine kinase
AU Ghosh, Sutapa; Zheng, Yaguo; Jun, Xiao; Mahajan, Sandeep; Mao, Chen; Sudbeck, Elise A.; **Uckun, Fatih M.**
CS Parker **Hughes** Cancer Center, Departments of Structural Biology, **Hughes Institute**, St.Paul, MN, 55113, USA
SO Clinical Cancer Research (1999), 5(12), 4264-4272
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
AB The epidermal growth factor receptor (EGFR) tyrosine kinase has an essential function for the survival of human breast cancer cells. In a systematic effort to design potent and specific inhibitors of this receptor family protein tyrosine kinase (PTK) as antibreast cancer agents, we recently reported the construction of a three-dimensional homol. model of the EGFR kinase domain. In this model, the catalytic site is defined by two β-sheets that form an interface at the cleft between the NH2-terminal and COOH-terminal lobes of the kinase domain. Our modeling studies revealed a distinct, remarkably planar triangular binding pocket within the kinase domain with approx. dimensions of 15 Å + 12Å + 12Å, and the thickness of the binding pocket is .apprx.7Å with an estimated volume of .apprx.600 Å3 available for inhibitor binding. Mol. docking studies had identified α-cyano-β-hydroxy-β-methyl-N-[4-(trifluoromethoxy)phenyl]-p ropenamide (LFM-A12) as our lead inhibitor, with an estimated binding constant of 13 μM, which subsequently inhibited EGFR kinase in vitro with an IC50 value of 1.7 μM. LFM-A12 was also discovered to be a highly specific inhibitor of the EGFR. Even at very high concns. ranging from

175-350 μM, this inhibitor did not affect the enzymic activity of other PTKs, including the Janus kinases **JAK1** and **JAK3**, the Src family kinase HCK, the Tec family member Bruton's tyrosine kinase, SYK kinase, and the receptor family PTK insulin receptor kinase. This observation is in contrast to the activity of a quinazoline inhibitor tested as a control, 4-(3-bromo, 4-hydroxyanilino)-6,7-dimethoxyquinazoline, which was shown to inhibit EGFR and other tyrosine kinases such as HCK, **JAK3**, and SYK.

IT **211555-04-3**, **WHI-P154**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epidermal growth factor receptor tyrosine kinase inhibitor LFM-A12)
RN 211555-04-3 HCAPLUS
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **152478-56-3**, Janus kinase 1 **152478-57-4**, Janus kinase 2
157482-36-5, **Janus kinase 3**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(epidermal growth factor receptor tyrosine kinase inhibitor LFM-A12)
RN 152478-56-3 HCAPLUS
CN Kinase (phosphorylating), JAK1 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 152478-57-4 HCAPLUS
CN Kinase (phosphorylating), JAK2 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

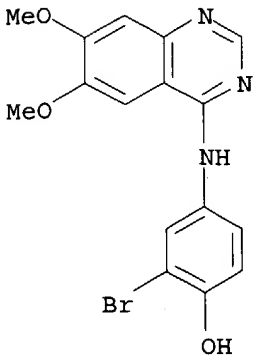
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Bacon, D	1988	6	219	J Mol Graphics	
Bohm, H	1992	6	593	J Comput Aided Mol D	MEDLINE
Bohm, H	1994	8	243	J Comput Aided Mol D	MEDLINE
Bridges, A	1996	39	267	J Med Chem	HCAPLUS
Carpenter, G	1990	265	7709	J Biol Chem	HCAPLUS
Chrysogelos, S	1994	29	29	Breast Cancer Res Tr	MEDLINE
Earp, H	1995	35	115	Cancer Res Treat	HCAPLUS
Fox, S	1994	29	41	Breast Cancer Res Tr	MEDLINE
Fry, D	1995	6	662	Curr Opin Biotechnol	HCAPLUS

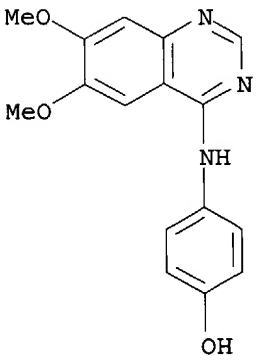
Fry, D	1998	95	12022	Proc Natl Acad Sci U	HCAPLUS
Fry, D	1994	265	1093	Science (Washington	HCAPLUS
George-Nascimento, C	1988	27	797	Biochemistry	HCAPLUS
Ghosh, S	1998	4	2657	Clin Cancer Res	HCAPLUS
Goodman, P	1998	273	17742	J Biol Chem	HCAPLUS
Hubbard, S	1997	16	5572	EMBO J	HCAPLUS
Khazaie, K	1993	12	255	Cancer Metastasis Re	HCAPLUS
Kraulis, P	1991	24	946	J Appl Crystallogr	
Mahajan, S	1999	274	9587	J Biol Chem	HCAPLUS
Mahajan, S	1995	15	5304	Mol Cell Biol	HCAPLUS
Mattar, T	1993	334	161	FEBS Lett	HCAPLUS
Mendelsohn, J	1995		607	Biologic Therapy of	
Merritt, E	1994	D50	869	Acta Crystallogr	HCAPLUS
Mohammadi, M	1997	276	955	Science (Washington	HCAPLUS
Moyer, J	1997	57	4838	Cancer Res	HCAPLUS
Narla, R	1998	4	1405	Clin Cancer Res	HCAPLUS
Rowley, R	1995	270	12659	J Biol Chem	HCAPLUS
Saouaf, S	1995	270	27072	J Biol Chem	HCAPLUS
Sicheri, F	1997	385	602	Nature (Lond)	HCAPLUS
Sudbeck, E	1999	5	1569	Clin Cancer Res	HCAPLUS
Toi, M	1991	27	977	Eur J Cancer	MEDLINE
Traxler, P	1997	40	3601	J Med Chem	HCAPLUS
Uckun, F	1998	4	901	Clin Cancer Res	HCAPLUS
Uckun, F	1995	267	886	Science (Washington	MEDLINE
Uckun, F	1996	22	1096	Science (Washington	
Vassilev, A	1999	274	1646	J Biol Chem	HCAPLUS
Wakeling, A	1996	38	67	Breast Cancer Res Tr	HCAPLUS
Wright, J	1995	270	12085	J Biol Chem	HCAPLUS
Xu, X	1996	52	527	Biochem Pharmacol	HCAPLUS
Yarden, Y	1988	57	443	Annu Rev Biochem	HCAPLUS
Zheng, J	1993	D49	362	Acta Crystallogr	HCAPLUS

L58 ANSWER 22 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:12537 HCAPLUS
DN 132:231841
TI A Specific Inhibitor of **Janus Kinase-3** Increases Survival in a Transgenic Mouse Model of Amyotrophic Lateral Sclerosis
AU Trieu, Vuong N.; Liu, Rugao; Liu, Xing-Ping; **Uckun, Fatih M.**
CS Drug Discovery Program, **Hughes Institute**, Roseville, MN, 55113, USA
SO Biochemical and Biophysical Research Communications (2000), 267(1), 22-25
CODEN: BBRCA9; ISSN: 0006-291X
PB Academic Press
DT Journal
LA English
AB Amyotrophic lateral sclerosis (ALS) is a progressive, fatal neurodegenerative disorder involving the motor neurons of cortex, brain stem, and spinal cord. About 10% of all ALS patients are familial cases (FALS), of which 20% have mutations in the Cu,Zn-superoxide dismutase (SOD1) gene. The murine model for FALS, which overexpresses a FALS variant of the SOD1 gene, exhibits progressive limbic paralysis followed by death. Treatment of FALS mice with **WHI-P131**, a specific inhibitor of **Janus kinase 3** (**JAK3**), increased survival by more than two months, suggesting that specific inhibitors of **JAK3** may be useful in the treatment of human ALS. These results uniquely establish **JAK3** as a novel mol. target for the treatment of FALS. (c) 2000 Academic Press.
IT **211555-04-3**, **WHI-P154**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(dimethoxyquinazoline inhibitors of **JAK3 kinase** increase survival in transgenic mouse model of amyotrophic lateral

sclerosis)
RN 211555-04-3 HCAPLUS
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **202475-60-3, WHI-P131**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dimethoxyquinazoline inhibitors of **JAK3 kinase** increase survival in transgenic mouse model of amyotrophic lateral sclerosis)
RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **157482-36-5, Janus kinase 3**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(dimethoxyquinazoline inhibitors of **JAK3 kinase** increase survival in transgenic mouse model of amyotrophic lateral sclerosis)
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RETABLE

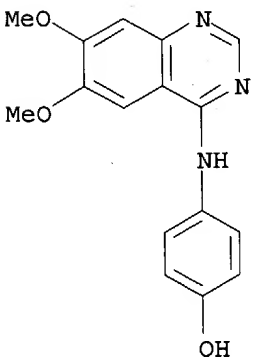
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Deng, H	1993	261	1047	Science	HCAPLUS
Eilers, A	1998	18	1713	J Neurosci	HCAPLUS

Estus, S	1994	127	1717	J Cell Biol	HCAPLUS
Fridovich, I	1986	58	61	Adv Enzymol	HCAPLUS
Glicksman, M	1998	35	361	J Neurobiol	HCAPLUS
Goodman, P	1998	273	17742	J Biol Chem	HCAPLUS
Gurney, M	1997	244	S15	J Neurol	
Gurney, M	1994	264	1772	Science	HCAPLUS
Hamida, M	1990	113	347	Brain	
Jaarsma, D	1996	219	179	Neurosci Lett	HCAPLUS
Kong, J	1998	18	3241	J Neuorosci	HCAPLUS
Kostic, V	1997	277	559	Science	HCAPLUS
Liu, R	1999	151	133	Radiation Res	HCAPLUS
Malaviya, R	1999	274	27028	J Biol Chem	HCAPLUS
Maroney, A	1998	18	104	J Neurosci	HCAPLUS
Migheli, A	1997	56	1314	J Neuropath Exp Neur	MEDLINE
Miller, N	1996	2	161	Redox Report	HCAPLUS
Mourelatos, Z	1996	93	5472	Proc Natl Acad Sci U	HCAPLUS
Mulder, D	1982		15	Human Motor Neuron D	MEDLINE
Narla, R	1998	4	1405	Clin Cancer Res	HCAPLUS
Rosen, D	1993	362	59	Nature	HCAPLUS
Siddique, T	1991	324	1381	N Engl J Med	MEDLINE
Sudbeck, E	1999	5	1569	Clin Cancer Res	HCAPLUS
Trieu, V	1998	247	277	Biochem Biophys Res	HCAPLUS
Trieu, V	1999	258	685	Biochem Biophys Res	HCAPLUS
Trieu, V	1999	152	508	Radiation Res	HCAPLUS
Uckun, F	1999	5	2954	Clin Cancer Res	HCAPLUS
Uckun, F	1995	267	886	Science	MEDLINE
Virgo, L	1995	676	196	Brain Res	HCAPLUS
Watson, A	1998	18	751	J Neurosci	HCAPLUS
Wiedau-Pazos, M	1996	271	515	Science	HCAPLUS
Williams, D	1991	66	54	Mayo Clin Proc	MEDLINE
Wong, P	1995	14	1105	Neuron	HCAPLUS
Yim, M	1996	93	5709	Proc Natl Acad Sci U	HCAPLUS

L58 ANSWER 23 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:735691 HCAPLUS
DN 132:202585
TI In vivo toxicity and pharmacokinetic features of the **Janus kinase 3** inhibitor **WHI-P131** [**4-(4'hydroxyphenyl)-amino-6,7-dimethoxyquinazoline**]
AU **Uckun, Fatih M.**; Ek, Onur; Liu, Xin-Ping; Chen, Chun-Lin
CS Parker **Hughes** Cancer Center, Departments of Oncology, Immunology, Drug Discovery Program, **Hughes Institute**, St. Paul, MN, 55113, USA
SO Clinical Cancer Research (1999), 5(10), 2954-2962
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
AB **4-(4'Hydroxyphenyl)-amino-6,7-dimethoxyquinazoline** (**WHI-P131**) is a potent and selective inhibitor of the **Janus kinase 3**, which triggers apoptosis in human acute lymphoblastic leukemia (ALL) cells. In this preclin. study, we evaluated the pharmacokinetics and toxicity of **WHI-P131** in rats, mice, and cynomolgus monkeys. Following i.v. administration, the terminal elimination half-life of **WHI-P131** was 73.2 min in rats, 103.4 min in mice, and 45.0 min in monkeys. The i.v. administered **WHI-P131** showed a very wide tissue distribution in mice. Following i.p. administration, **WHI-P131** was rapidly absorbed in both rats and mice, and the time to reach the maximum plasma concentration (tmax) was 24.8 min in rats and 10.0 min in mice. Subsequently, **WHI-P131** was eliminated with a terminal elimination

half-life of 51.8 min in rats and 123.6 min in mice. The estimated i.p. bioavailability was 95% for rats, as well as for mice. **WHI-P131** was quickly absorbed after oral administration in mice with a tmax of 5.8 min, but its oral bioavailability was relatively low (29.6%). The elimination half-life of **WHI-P131** after oral administration was 297.6 min. **WHI-P131** was not acutely toxic to mice at single i.p. bolus doses ranging from 0.5-250 mg/kg. Two cynomolgus monkeys treated with 20 mg/kg **WHI-P131** and one cynomolgus monkey treated with 100 mg/kg **WHI-P131** experienced no side effects. Plasma samples from **WHI-P131**-treated monkeys exhibited potent antileukemic activity against human ALL cells in vitro. To our knowledge, this is the first preclin. toxicity and pharmacokinetic study of a **Janus kinase 3** inhibitor. Further development of **WHI-P131** may provide the basis for new and effective treatment programs for relapsed ALL in clin. settings.

IT **202475-60-3, WHI-P131**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(in vivo toxicity and pharmacokinetic features of the **Janus kinase 3** inhibitor **WHI-P131**)
RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **157482-36-5, Janus kinase 3**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(in vivo toxicity and pharmacokinetic features of the **Janus kinase 3** inhibitor **WHI-P131**)
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Boxenbaum, H	1984	15	1071	Drug Metab Rev	HCAPLUS
Chen, C	1999	727	205	J Chromatogr B (Biom	HCAPLUS
Chen, C	1999	16	1003	Pharm Res	HCAPLUS
Chen, C	1999	16	117	Pharm Res	HCAPLUS
Davies, B	1993	10	1093	Pharm Res	MEDLINE
Demoulin, J	1996	16	4710	Mol Cell Biol	HCAPLUS
Gouilleux-Gruart, V	1996	87	1692	Blood	HCAPLUS
Ihle, J	1995	60	1	Adv Immunol	HCAPLUS

Jodrell, D	1991	28	331	Cancer Chemother Pha	HCAPLUS
Jurlander, J	1997	89	4146	Blood	HCAPLUS
Kaneko, S	1997	109	185	Clin Exp Immunol	HCAPLUS
Messinger, Y	1998	4	165	Clin Cancer Res	HCAPLUS
Nakamura, N	1996	271	19483	J Biol Chem	HCAPLUS
Obach, R	1997	283	46	J Pharmacol Exp Ther	HCAPLUS
Ritschel, W	1992	103	249	Comp Biochem Physiol	MEDLINE
Sudbeck, E	1999	5	1569	Clin Cancer Res	HCAPLUS
Uckun, F	1998	4	1125	Clin Cancer Res	HCAPLUS
Uckun, F	1995	267	886	Science (Washington	MEDLINE
Weber-Nordt, R	1996	88	809	Blood	HCAPLUS
Witthuhn, B	1999	32	289	Leuk Lymphoma	MEDLINE

L58 ANSWER 24 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:661331 HCAPLUS
DN 132:145960
TI Recent advances in **JAK3 kinase** inhibitors
AU Sudbeck, Elise A.; **Uckun, Fatih M.**
CS Parker **Hughes** Cancer Center, **Hughes Institute**
, St Paul, MN, 55113, USA
SO IDrugs (1999), 2(10), 1026-1030
CODEN: IDRUFN; ISSN: 1369-7056
PB Current Drugs Ltd.
DT Journal; General Review
LA English
AB A review with 59 refs. The Janus family of tyrosine kinases (**JAKs**
) has emerged as a promising target for therapeutic agents. **JAKs**
are involved in pathways which help regulate cellular functions in the
lympho-hematopoietic system critical for cell proliferation and cell
survival. **JAKs** are abundantly expressed in primary leukemic
cells from children with acute lymphoblastic leukemia (ALL) and are
involved in signals regulating apoptosis. Two recently reported
dimethoxyquinazoline compds., **WHI-P131** and **WHI**
-P154 (Hughes Institute), were found to inhibit **JAK3**
but not **JAK1** or **JAK2.** The high potency and
selectivity of **WHI-P131** for **JAK3** makes it a
promising candidate for new treatment strategies against ALL, the most
common form of childhood cancer. In addition to its antileukemic properties,
WHI-P131 also shows clin. potential for the treatment of
mast cell-mediated immediate hypersensitivity reactions and allergic
disorders, including asthma, as well as immunosuppression of alloimmune
and autoimmune disorders.
IT **157482-36-5, JAK3 kinase**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU
(Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(recent advances in **JAK3 kinase** inhibitors)
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RETABLE

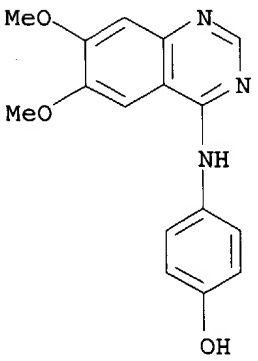
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Boussiotis, V	1994	266	1039	Science	HCAPLUS
Bunjes, D	1981	11	657	Eur J Immunol	HCAPLUS
Caravatti, G	1994	4	399	Bioorg Med Chem Lett	HCAPLUS
Cetkovic-Cvrlje, M	1999			Transplantation, sub	
Chen, M	1997	94	6910	Proc Natl Acad Sci U	HCAPLUS
Demoulin, J	1996	16	4710	Mol Cell Biol	HCAPLUS
Fiorucci, G	1995	69	5833	J Virol	HCAPLUS
Frank, S	1994	270	776	Endocrinology	
Frank, S	1995	270	776	J Biol Chem	

Fujita-Yamaguchi, Y	1988	157	955	Biochem Biophys Res	HCAPLUS
Galli, S	1993	328	257	New Engl J Med	MEDLINE
Ghosh, S	1998	4	2657	Clin Cancer Res	HCAPLUS
Gordon, J	1990	346	274	Nature	HCAPLUS
Hamawy, M	1995	7	535	Cell Signal	HCAPLUS
Harpur, A	1992	7	1347	Oncogene	HCAPLUS
Harris, D	1999	23	137	Bone Marrow Transpla	MEDLINE
Horvath, C	1997	9	233	Curr Opin Cell Biol	HCAPLUS
Hubbard, S	1997	16	5572	EMBO J	HCAPLUS
Imami, N	1998	65	979	Transplantation	HCAPLUS
Johnston, J	1994	370	151	Nature	HCAPLUS
Jurlander, J	1997	89	4146	Blood	HCAPLUS
Kaneko, S	1997	109	185	Clin Exp Immun	HCAPLUS
Kohlhuber, F	1997	17	695	Mol Cell Biol	HCAPLUS
Krolewski, J	1990	5	277	Oncogene	HCAPLUS
Lamers, M	1999	285	713	J Mol Biol	HCAPLUS
Leonard, W	1998	16	293	Annu Rev Immunol	HCAPLUS
Leonard, W	1996	47	229	Annu Rev Med	HCAPLUS
Levy, D	1997	8	81	Cytokine Growth Fact	HCAPLUS
Li, X	1998	161	890	J Immunol	HCAPLUS
Liu, K	1998	10	271	Curr Opin Immunol	HCAPLUS
Mahajan, S	1999	274	9587	J Biol Chem	HCAPLUS
Malaviya, R	1999	257	807	Biochem Biophys Res	HCAPLUS
Malaviya, R	1999	103	S58	J Allergy Clin Immun	
Malaviya, R	1993	268	4939	J Biol Chem	HCAPLUS
Malaviya, R	1999			to be published in J	
Manna, S	1999	162	2095	J Immunol	HCAPLUS
Mattar, T	1993	334	161	FEBS Lett	HCAPLUS
Meggio, F	1995	234	317	Eur J Biochem	HCAPLUS
Meydan, N	1996	379	645	Nature	HCAPLUS
Miyazaki, T	1994	266	1045	Science	HCAPLUS
Nakamura, N	1996	271	19483	J Biol Chem	HCAPLUS
Nakano, H	1987	40	706	J Antibiot	HCAPLUS
Nielsen, M	1997	94	6764	Proc Natl Acad Sci U	HCAPLUS
Noguchi, M	1993	73	147	Cell	HCAPLUS
Prade, L	1997	5	1627	Structure	HCAPLUS
Russell, S	1994	266	1042	Science	HCAPLUS
Sicheri, F	1997	385	602	Nature	HCAPLUS
Siemasko, K	1998	160	1581	J Immunol	HCAPLUS
Sudbeck, E	1999	5	1569	Clin Cancer Res	HCAPLUS
Sugamura, K	1996	14	179	Annu Rev Immunol	HCAPLUS
Takahashi, T	1994	342	124	FEBS Lett	HCAPLUS
Takemoto, S	1997	94	13897	Proc Natl Acad Sci U	HCAPLUS
Tortolani, P	1995	155	5220	J Immunol	HCAPLUS
Wang, L	1999	162	3897	J Immunol	HCAPLUS
Wasik, M	1998	28	551	Leuk Lymphoma	MEDLINE
Wilks, A	1991	11	2057	Mol Cell Biol	HCAPLUS
Witthuhn, B	1999	32	289	Leuk Lymphoma	MEDLINE
Witthun, B	1994	370	153	Nature	
Yamashita, N	1997	50	440	J Antibiot (Tokyo)	HCAPLUS
Zhang, Q	1996	93	9148	Proc Natl Acad Sci U	HCAPLUS
Zhao, Y	1995	270	814	J Biol Chem	

L58 ANSWER 25 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:622744 HCAPLUS
DN 131:309757
TI Targeting **Janus kinase 3** in mast cells prevents immediate hypersensitivity reactions and anaphylaxis
AU Malaviya, Ravi; Zhu, DeMin; Dibirdik, Ilker; **Uckun, Fatih M.**
CS Department of Allergy, **Hughes Institute**, St. Paul, MN, 55113, USA
SO Journal of Biological Chemistry (1999), 274(38), 27028-27038
CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB **Janus kinase 3** (**JAK3**), a member of the Janus family protein-tyrosine kinases, is expressed in mast cells, and its enzymic activity is enhanced by IgE receptor/FcεRI crosslinking. Selective inhibition of **JAK3** in mast cells with **4-(4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline** (**WHI-P131**) blocked the phospholipase C activation, calcium mobilization, and activation of microtubule-associated protein kinase after IgE receptor/FcεRI crosslinking. Treatment of IgE-sensitized rodent as well as human mast cells with **WHI-P131** effectively inhibited the activation-associated morphol. changes, degranulation, and proinflammatory mediator release after specific antigen challenge without affecting the functional integrity of the distal secretory machinery. In vivo administration of the **JAK3** inhibitor **WHI-P131** prevented mast cell degranulation and development of cutaneous as well as systemic fatal anaphylaxis in mice at nontoxic dose levels. Thus, **JAK3** plays a pivotal role in IgE receptor/FcεRI-mediated mast cell responses, and targeting **JAK3** with a specific inhibitor, such as **WHI-P131**, may provide the basis for new and effective treatment as well as prevention programs for mast cell-mediated allergic reactions.
IT **157482-36-5, JAK3 protein kinase**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(targeting **JAK3** in mast cells prevents immediate hypersensitivity reactions and anaphylaxis)
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **202475-60-3, WHI-P131**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeting **JAK3** in mast cells prevents immediate hypersensitivity reactions and anaphylaxis)
RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File

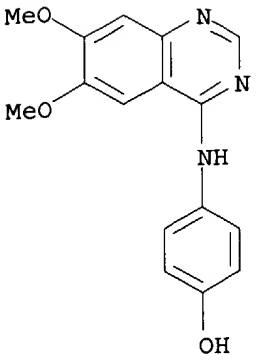
Amir, S	1991	203	125	Eur J Pharmacol	HCAPLUS
Apgar, J	1997	110	771	J Cell Sci	HCAPLUS
Blank, U	1989	337	187	Nature	HCAPLUS
Buckley, R	1997	130	378	J Pediatr	MEDLINE
Costello, P	1996	13	2595	Oncogene	HCAPLUS
Darnell, J	1994	264	1415	Science	HCAPLUS
Dibirdik, I	1998	273	4035	J Biol Chem	HCAPLUS
Endo, T	1997	387	921	Nature	HCAPLUS
Galli, S	1993	328	257	N Engl J Med	MEDLINE
Ghosh, S	1999	47	121	Clin Cancer Res	
Goodman, P	1998	273	17742	J Biol Chem	HCAPLUS
Gordon, J	1990	346	274	Nature	HCAPLUS
Hamawy, M	1995	7	535	Cell Signalling	HCAPLUS
Hirasawa, N	1995	270	10960	J Biol Chem	HCAPLUS
Hogan, A	1997	13	43	Methods	HCAPLUS
Ihle, J	1996	351	159	Philos Trans R Soc L	HCAPLUS
Ihle, J	1995	11	69	Trends Genet	HCAPLUS
Irani, A	1989	37	1509	J Histochem Cytochem	MEDLINE
Levy, D	1997	8	81	Cytokine Growth Fact	HCAPLUS
Liu, F	1980	124	2728	J Immunol	HCAPLUS
Mahajan, S	1999	274	9587	J Biol Chem	HCAPLUS
Malaviya, R	1999	257	807	Biochem Biophys Res	HCAPLUS
Malaviya, R	1993	268	4939	J Biol Chem	HCAPLUS
Malaviya, R	1994	93	1645	J Clin Invest	MEDLINE
Malaviya, R	1996	106	785	J Invest Dermatol	HCAPLUS
Malaviya, R	1995	253	27	Methods Enzymol	MEDLINE
Malaviya, R	1996	381	77	Nature	HCAPLUS
Millard, P	1989	264	19730	J Biol Chem	HCAPLUS
Miyajima, I	1997	99	901	J Clin Invest	HCAPLUS
Miyazaki, T	1996	27	25	Cancer Surveys	HCAPLUS
Narla, R	1998	4	1405	Clin Cancer Res	HCAPLUS
Nelson, B	1996	16	369	Mol Cell Biol	
Nosaka, T	1995	270	800	Science	HCAPLUS
Oettgen, H	1994	370	367	Nature	HCAPLUS
Oliver, J	1994	269	29697	J Biol Chem	HCAPLUS
Ozawa, K	1993	268	1749	J Biol Chem	HCAPLUS
Riske, F	1991	266	11245	J Biol Chem	HCAPLUS
Scharenberg, A	1995	14	3385	EMBO J	HCAPLUS
Siraganian, R	1998	1	204	Allergy Principles a	
Sudbeck, E	1999	5	1569	Clin Cancer Res	HCAPLUS
Thomis, D	1995	270	794	Science	HCAPLUS
Uckun, F	1988	71	13	Blood	MEDLINE
Uckun, F	1998	4	901	Clin Cancer Res	HCAPLUS
Uckun, F	1991	88	3589	Proc Natl Acad Sci U	HCAPLUS
Uckun, F	1995	267	886	Science	MEDLINE
Uckun, F	1996	273	1096	Science	HCAPLUS
Villa, A	1996	88	817	Blood	HCAPLUS
Wei, Y	1986	137	1993	J Immunol	HCAPLUS
Witthuhn, B	1999	32	289	Lymphoma Leukemian	MEDLINE
Wong, A	1992	31	4046	Biochemistry	HCAPLUS
Xia, H	1997	159	2911	J Immunol	HCAPLUS
Zhang, J	1996	184	71	J Exp Med	HCAPLUS
Zhu, D	1998	4	2967	Clin Cancer Res	HCAPLUS

L58 ANSWER 26 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:428003 HCAPLUS
DN 131:295193
TI Structure-based design of specific inhibitors of **janus kinase 3** as apoptosis-inducing antileukemic agents
AU Sudbeck, Elise A.; Liu, Xing-Ping; Narla, Rama Krishna; Mahajan, Sandeep; Ghosh, Sutapa; Mao, Chen; **Uckun, Fatih M.**
CS Parker **Hughes** Cancer Center, **Hughes Institute**, St. Paul, MN, 55113, USA

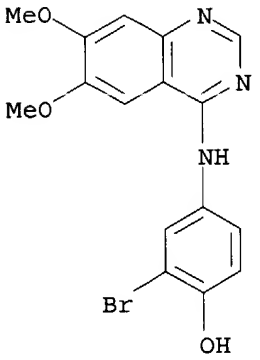
SO Clinical Cancer Research (1999), 5(6), 1569-1582
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
AB A novel homol. model of the kinase domain of Janus kinase (**JAK**) **3** was used for the structure-based design of dimethoxyquinazoline compds. with potent and specific inhibitory activity against **JAK3**. The active site of **JAK3** in this homol. model measures roughly 8 Å + 11 Å + 20 Å, with a volume of .apprx.530 Å3 available for inhibitor binding. Modeling studies indicated that 4-(phenylamino)-6,7-dimethoxyquinazoline (WHI-258) (I) would likely fit into the catalytic site of **JAK3** and that derivs. of I that contain an OH group at the 4' position of the Ph ring would more strongly bind to **JAK3** because of added interactions with Asp-967, a key residue in the catalytic site of **JAK3**. These predictions were consistent with docking studies indicating that compds. containing a 4-OH group, **WHI-P131** [4-((4-**hydroxyphenyl**)**amino**)-6,7-**dimethoxyquinazoline**], **WHI-P154** [4-((3-**bromo-4-hydroxyphenyl**)**amino**)-6,7-**dimethoxyquinazoline**], and WHI-P97 [4-((3,5-dibromo-4-hydroxyphenyl)amino)-6,7-dimethoxyquinazoline], were likely to bind favorably to **JAK3**, with estimated Kis ranging from 0.6 to 2.3 μM. These compds. inhibited **JAK3** in immune complex kinase assays in a dose-dependent fashion. In contrast, compds. lacking the 4-OH group, WHI-P79 [4-((3-bromophenyl)amino)-6,7-dimethoxyquinazoline], WHI-P111 [4-((3-bromo-4-methylphenyl)amino)-6,7-dimethoxyquinazoline], WHI-P112 [4-((2,5-dibromophenyl)amino)-6,7-dimethoxyquinazoline], WHI-P132 [4-((2-hydroxyphenyl)amino)-6,7-dimethoxyquinazoline], and WHI-P258 [4-(phenylamino)-6,7-dimethoxyquinazoline], were predicted to bind less strongly, with estimated Kis ranging from 28 to 72 μM. These compds. did not show any significant **JAK3** inhibition in kinase assays. Furthermore, the lead dimethoxyquinazoline compound, **WHI-P131**, which showed potent **JAK3**-inhibitory activity (IC50 of 78 μM), did not inhibit **JAK1** and **JAK2**, the ZAP/SYK family tyrosine kinase SYK, the TEC family tyrosine kinase BTK, the SRC family tyrosine kinase LYN, or the receptor family tyrosine kinase insulin receptor kinase, even at concns. as high as 350 μM. **WHI-P131** induced apoptosis in **JAK3**-expressing human leukemia cell lines NALM-6 and LC1;19 but not in melanoma (M24-MET) or squamous carcinoma (SQ20B) cells. Leukemia cells were not killed by dimethoxyquinazoline compds. that were inactive against **JAK3**. **WHI-P131** inhibited the clonogenic growth of **JAK3**-pos. leukemia cell lines DAUDI, RAMOS, LC1;19, NALM-6, MOLT-3, and HL-60 (but not **JAK3**-neg. BT-20 breast cancer, M24-MET melanoma, or SQ20B squamous carcinoma cell lines) in a concentration-dependent fashion. Potent and specific inhibitors of **JAK3** such as **WHI-P131** may provide the basis for the design of new treatment strategies against acute lymphoblastic leukemia, the most common form of childhood cancer.

IT **202475-60-3**, **WHI-P131** **211555-04-3**, **WHI-P154**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structure-based design of specific inhibitors of **janus kinase 3** as apoptosis-inducing antileukemic agents)

RN 202475-60-3 HCAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 211555-04-3 HCAPLUS
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



IT **157482-36-5, JAK3 kinase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(structure-based design of specific inhibitors of **janus kinase 3** as apoptosis-inducing antileukemic agents)
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Bohm, H	1994	8	243	J Comput Aided Mol D	MEDLINE
Brunger, A	1992			A System for X-Ray C	
Bushkin, I	1990	172	676	Biochem Biophys Res	HCAPLUS
Demoulin, J	1996	16	4710	Mol Cell Biol	HCAPLUS
D'Cruz, O	1998	58	1515	Biol Reprod	HCAPLUS
Fujii, H	1997	29	571	Histochem J	HCAPLUS
Ghosh, S	1998	4	2657	Clin Cancer Res	HCAPLUS
Goodman, P	1998	273	17742	J Biol Chem	HCAPLUS
Horvath, C	1997	9	233	Curr Opin Cell Biol	HCAPLUS
Hubbard, S	1997	16	5572	EMBO J	HCAPLUS
Hubbard, S	1994	372	746	Nature (Lond)	HCAPLUS
Ihle, J	1995	60	1	Adv Immunol	HCAPLUS
Jurlander, J	1997	89	4146	Blood	HCAPLUS
Kaneko, S	1997	109	185	Clin Exp Immunol	HCAPLUS
Kaplan, G	1989	159	1275	Biochem Biophys Res	HCAPLUS

Kristupaitis, D	1998	273	9119	J Biol Chem	
Levy, D	1997	8	81	Cytokine Growth Fact	HCAPLUS
Maftah, A	1989	164	185	Biochem Biophys Res	HCAPLUS
Mahajan, S	1999	274	9587	J Biol Chem	HCAPLUS
Mahajan, S	1995	15	5304	Mol Cell Biol	HCAPLUS
Mancini, M	1997	138	449	J Cell Biol	HCAPLUS
Messinger, Y	1998	4	165	Clin Cancer Res	HCAPLUS
Meydan, N	1996	379	645	Nature (Lond)	HCAPLUS
Mohammadi, M	1996	86	577	Cell	HCAPLUS
Mohammadi, M	1997	276	955	Science (Washington	HCAPLUS
Nakamura, N	1996	271	19483	J Biol Chem	HCAPLUS
Narla, R	1998	4	1405	Clin Cancer Res	HCAPLUS
Newman, J	1992	50	500	Int J Cancer	HCAPLUS
Petit, P	1995	130	157	J Cell Biol	HCAPLUS
Rewcastle, G	1995	38	3482	J Med Chem	HCAPLUS
Sack, J	1988	6	244	J Mol Graphics	
Sicheri, F	1997	385	602	Nature (Lond)	HCAPLUS
Smiley, S	1991	88	3671	Proc Natl Acad Sci U	HCAPLUS
Uckun, F	1998	4	901	Clin Cancer Res	HCAPLUS
Uckun, F	1996	271	6396	J Biol Chem	
Uckun, F	1986	163	347	J Exp Med	HCAPLUS
Uckun, F	1995	267	886	Science (Washington	MEDLINE
Uckun, F	1996	22	1096	Science (Washington	
Vassilev, A	1999	274	1646	J Biol Chem	HCAPLUS
Witthuhn, B	1999	32	289	Leuk Lymphoma	MEDLINE
Xiao, J	1996	271	7659	J Biol Chem	MEDLINE
Zhu, D	1998	4	2967	Clin Cancer Res	HCAPLUS

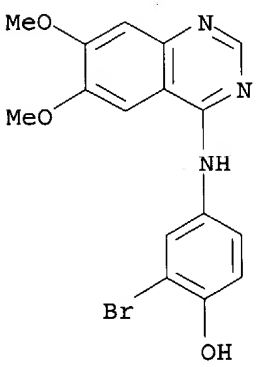
L58 ANSWER 27 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:404065 HCAPLUS
DN 131:179230
TI A quantitative HPLC detection method for **WHI-P154** [**4-(3'-bromo-4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline**]
AU Chen, C. L.; Narla, R. K.; Liu, X. P.; **Uckun, F. M.**
CS Parker **Hughes** Cancer Center, Department of Molecular Pharmacology, **Hughes Institute**, St. Paul, MN, 55113, USA
SO Journal of Liquid Chromatography & Related Technologies (1999), 22(11), 1771-1783
CODEN: JLCTFC; ISSN: 1082-6076
PB Marcel Dekker, Inc.
DT Journal
LA English
AB **WHI-P154** [**4-(3'-bromo-4'hydroxylphenyl)-amino-6,7 dimethoxyquinazoline**] is a novel anti-tumor agent with unique cytotoxic activity against human glioblastoma cells (Clin. Cancer. Res. 4:1405-1414, 1998). Further development of **WHI-P154** will require detailed pharmacodynamic studies in preclin. animal models. Therefore, we established a sensitive and accurate high performance liquid chromatog. (HPLC)-based quant. detection method for **WHI-P154.** This method allows the measurement of **WHI-P154** levels in plasma, as well as in target human glioblastoma cells. Plasma and cell lysates were extracted with chloroform, dried with nitrogen gas and reconstituted in methanol: water (9:1, volume/volume). An aliquot was injected into a Hewlett Packard HPLC system employing a 250+4 mm Lichrospher 100, RP-18 (5 μm) anal. column in conjunction with a 4+4 mm Lichrospher 100, RP-18 (5 μm) guard column. The eluted compds. were detected by a diode array detector set at a wavelength of 335 nm. Acetonitrile/water containing 0.1% trifluoroacetic acid and 0.1% triethylamine (28:72, volume/volume) was used as a mobile phase.

The average extraction recovery of **WHI-P154** was 78.3% for plasma and 96.0% for U373 human glioblastoma cells. The assay was linear (r>0.999) within the concentration range of 0.1-20 μM in 100 μL plasma and within the quantity range of 0.025-5 nmol per 2.5 million U373 glioblastoma cells. The intra- and inter-assay variabilities were less than 6% and the lowest detection limit of **WHI-P154** was 0.05 μM in plasma and 0.01 nmol in U373 cells, resp. The practical utility of this new HPLC method was confirmed in pilot pharmacokinetic studies using rats as well as cellular uptake studies using U373 human glioblastoma cells.

IT **211555-04-3, WHI-P154**
RL: ANT (Analyte); ANST (Analytical study)
(quant. HPLC detection method for **WHI-P154**)

RN 211555-04-3 HCAPLUS

CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Berens, M	1990	1	1	Neurosurg Clinics N	MEDLINE
Brandes, A	1996	14	551	Cancer Invest	HCAPLUS
Chen, C	1993	26	1125	Analytical Letters	HCAPLUS
Chen, C	1993	9	429	Analytical Sciences	HCAPLUS
Chen, C	1992	583	274	J Chromatogr Biomed	HCAPLUS
Chen, C	1994	17	3681	J Liquid Chromatogr	HCAPLUS
Chen, C	1994	17	913	J Liquid Chromatogr	HCAPLUS
Chintala, S	1996	14	358	Clin Exp Metastasis	HCAPLUS
Devaux, B	1993	78	767	J Neurosurg	MEDLINE
Finlay, J	1992		278	Pediatric Neuro-Onco	
Grossman, S	1995	22	530	Sem Oncol	HCAPLUS
Kreth, F	1993	78	762	J Neurosurg	MEDLINE
Narla, R	1998	4	1405	Clin Cancer Res	HCAPLUS
Narla, R	1998	4	2463	Clin Cancer Res	HCAPLUS
Pardos, M	1997	I	1471	Cancer Medicine	
Pardos, M	1998	14	88	Sem Surgical Oncol	
Quigley, N	1991	29	385	Neurosurgery	
Russel, D	1989		83	Pathology of Tumors	
WinNonlin, Scientific C	1995			User's Guide	

L58 ANSWER 28 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:341446 HCAPLUS

DN 131:96898

TI Quantitative high-performance liquid chromatographic method for pharmacokinetic studies of the potent mast cell inhibitor **4-(4'-hydroxyphenyl)amino-6,7**

-dimethoxyquinazoline (**WHI-P131**)

AU Chen, Chun-Lin; Malaviya, Ravi; Chen, Hao; Liu, Xing-Ping; **Uckun, Fatih M.**

CS Department of Pharmaceutical Sciences, **Hughes Institute**, St. Paul, MN, USA

SO Journal of Chromatography, B: Biomedical Sciences and Applications (1999), 727(1 + 2), 205-212
CODEN: JCBBEP; ISSN: 0378-4347

PB Elsevier Science B.V.

DT Journal

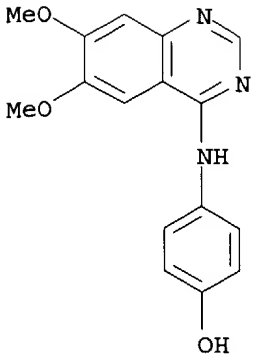
LA English

AB The novel quinazoline derivative **4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline** (**WHI-P131**) has recently been identified as a potent mast cell inhibitor capable of preventing IgE/antigen-induced cutaneous as well as systemic fatal anaphylaxis in mice. Here, the authors describe a sensitive high-performance liquid chromatog. (HPLC)-based quant. detection method for measurement of **WHI-P131** levels in plasma as well as in target mast cells. The average extraction recovery for **WHI-P131** was 88.4% for plasma and 75.7% for RBL-2H3 mast cell lysates. Good linearity (r>0.999) was observed throughout the concentration range of 0.1-20 μM in plasma and 0.01-5 nmol in 5·106 cells (0.5-238 μM per cell) for **WHI-P131.** Intra- and interassay variabilities were <7% and the lowest detection limit of **WHI-P131** was 0.05 μM in plasma and 0.005 nmol in 5 million cells, resp., at a signal-to-noise ratio of .apprx.2. The practical utility of this new HPLC method was confirmed in a pilot pharmacokinetic study in BALB/c mice as well as in a cellular drug uptake and disposition study in RBL-2H3 mast cells. After i.p. administration of a non-toxic 40 mg/kg bolus dose of **WHI-P131**, the estimated maximum plasma concentration was 92.7 μM, which is .apprx.1-log higher than the effective in vitro mast cell inhibitory concns. of **WHI-P131.** The drug absorption was rapid with an absorption half-life of only 2.9 min and the estimated time to reach the maximum plasma concentration was 8.3 min. **WHI-P131** was cleared with an apparent systemic clearance rate of 2586 mL/h/kg and an elimination half-life of 1.8 h. An intracellular exposure level (AUC) of 55 μM·h was obtained after in vitro treatment of RBL-2H3 mast cells with **WHI-P131** at a 33.6 μM final concentration in culture medium. The availability of the described quant. HPLC detection method for **WHI-P131** provides the basis for further development of **WHI-P131** as an anti-allergic drug through detailed pharmacodynamic studies in preclin. animal models.

IT **202475-60-3**, **WHI-P131**
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(high-performance liquid chromatog. method for pharmacokinetic studies of **WHI-P131**)

RN 202475-60-3 HCAPLUS

CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Anon	1997			User's Guide, WinNon	
Chen, C	1993	26	1125	Anal Lett	HCAPLUS
Chen, C	1993	9	42	Anal Sci	
Chen, C	1992	583	274	J Chromatogr	HCAPLUS
Chen, C	1994	17	3681	J Liq Chromatogr	HCAPLUS
Chen, C	1994	17	913	J Liq Chromatogr	HCAPLUS
Chen, C	1999	16	117	Pharm Res	HCAPLUS
Chen, C	1999			to be published in J	
Galli, S	1991	3	865	Curr Opin Immunol	HCAPLUS
Galli, S	1993	328	257	New Eng J Med	MEDLINE
Hamawy, M	1995	27	535	Cell Signal	
Narla, R	1998	4	1405	Clin Cancer Res	HCAPLUS
Narla, R	1998	4	2463	Clin Cancer Res	HCAPLUS
Scharenberg, A	1995	61	72	Chem Immunol	HCAPLUS
Uckun, F	1999	103	58	J Allergy and Clin I	

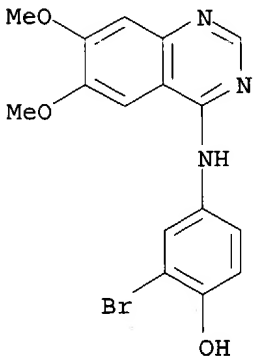
L58 ANSWER 29 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:242184 HCAPLUS
DN 131:72658
TI Genetic and Biochemical Evidence for a Critical Role of Janus Kinase (**JAK**)-**3** in Mast Cell-Mediated Type I Hypersensitivity Reactions
AU Malaviya, Ravi; **Uckun, Fatih M.**
CS Department of Allergy, **Hughes Institute**, St. Paul, MN, USA
SO Biochemical and Biophysical Research Communications (1999), 257(3), 807-813
CODEN: BBRCA9; ISSN: 0006-291X
PB Academic Press
DT Journal
LA English
AB We investigated the role of **JAK3** in IgE receptor/FcεRI-mediated mast cell responses. IgE/antigen induced degranulation and mediator release were substantially reduced with **Jak3**-/- mast cells from **JAK3**-null mice that were generated by targeted disruption of **Jak3** gene in embryonic stem cells. Further, treatment of mast cells with (3'bromo-4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (**WHI-P154**), a potent inhibitor of **JAK3**, inhibited degranulation and proinflammatory mediator release after IgE receptor/ FcεRI crosslinking. Thus, **JAK3** plays a pivotal role in IgE receptor/ FcεRI-mediated mast cell responses and targeting **JAK3** may provide the basis for new and effective treatment as well as prevention programs for mast cell-mediated

allergic reactions. (c) 1999 Academic Press.

IT **157482-36-5**
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(genetic and biochem. evidence for critical role of Janus Kinase (**JAK**)-**3** in mast cell-mediated type I hypersensitivity reactions)
RN 157482-36-5 HCAPLUS
CN Kinase (phosphorylating), JAK3 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **211555-04-3**, **Whi-p154**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(genetic and biochem. evidence for critical role of Janus Kinase (**JAK**)-**3** in mast cell-mediated type I hypersensitivity reactions and inhibition by)
RN 211555-04-3 HCAPLUS
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Apgar, J	1997	110	771	J Cell Sci	HCAPLUS
Blank, U	1989	337	187	Nature	HCAPLUS
Buckley, R	1997	130	378	J Pediatr	MEDLINE
Costello, P	1996	13	2595	Oncogene	HCAPLUS
Dvorak, A	1994	144	160	Am J Pathol	HCAPLUS
Galli, S	1993	328	257	New Eng J Med	MEDLINE
Ghosh, S	1999	47	121	Clin Cancer Res	
Goodman, P	1998	273	17742	J Biol Chem	HCAPLUS
Gordon, J	1990	346	274	Nature	HCAPLUS
Hamawy, M	1995	7	535	Cellular Signalling	HCAPLUS
Ihle, J	1995	11	69	Trends Genet	HCAPLUS
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Malaviya, R	1993	268	4939	J Biol Chem	HCAPLUS
Malaviya, R	1994	152	1907	J Immunol	HCAPLUS
Malaviya, R	1996	106	785	J Invest Dermatol	HCAPLUS
Malaviya, R	1996	381	77	Nature	HCAPLUS
Nosaka, T	1995	270	800	Science	HCAPLUS
Oliver, J	1994	269	29697	J Biol Chem	HCAPLUS
Ozawa, K	1993	268	1749	J Biol Chem	HCAPLUS
Scharenberg, A	1995	14	3385	EMBO J	HCAPLUS
Sudbeck, E	1999			to be published in C	
Thomis, D	1995	270	794	Science	HCAPLUS

Uckun, F	1998	4	901	Clin Cancer Res	HCAPLUS
Villa, A	1996	88	817	Blood	HCAPLUS
Wei, Y	1986	137	1993	J Immunol	HCAPLUS

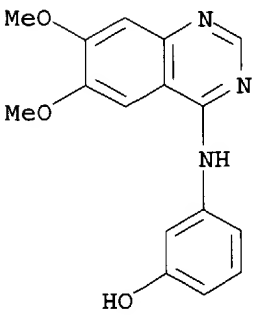
L58 ANSWER 30 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:92661 HCAPLUS
TI Microemulsion, liposome, and mixed micellar formulations for a poorly water soluble quinazoline derivative
AU Yiv, S. H.; Metz, M.; Li, M.; Liu, X-P.; **Uckun, F. M.**
CS **Hughes Institute, St. Paul, MN, 55113, USA**
SO Book of Abstracts, 217th ACS National Meeting, Anaheim, Calif., March 21-25 (1999), MEDI-148 Publisher: American Chemical Society, Washington, D. C.
CODEN: 67GHA6
DT Conference; Meeting Abstract
LA English
AB The purpose of this investigation was to develop an i.v. vehicle for an anti-leukemic quinazoline derivative, **4-(4'-Hydroxylphenyl)-amino-6,7-dimethoxyquinazoline** with potent and specific **Janus kinase 3** (**JAK3**) inhibitory activity. Several submicron lipid dispersed systems were evaluated with regard to their solubilizing capacity for this drug. Several components with known parenteral history were utilized with the objective to achieve the highest possible drug incorporation level in the vehicle. Based on the overall solubilization behavior, it was determined that, at the interface, the drug mols. reside closer to the hydrophilic environment than to the hydrophobic core. The highest solubilization was obtained with systems containing pegylated phospholipids. The solubilization enhancement caused by the presence of pegylated phospholipids was found in all three systems, microemulsion, micelle, and liposome.

L58 ANSWER 31 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:92573 HCAPLUS
TI Structural basis for potent and selective inhibition of **janus kinase 3** (**JAK3**) by anti-leukemic agent **WHI-P131**
AU Sudbeck, Elise A.; Liu, Xing-Ping; Mahajan, Sandeep; Mao, Chen; **Uckun, Fatih M.**
CS **Hughes Institute, St. Paul, MN, 55113, USA**
SO Book of Abstracts, 217th ACS National Meeting, Anaheim, Calif., March 21-25 (1999), MEDI-059 Publisher: American Chemical Society, Washington, D. C.
CODEN: 67GHA6
DT Conference; Meeting Abstract
LA English
AB Structure-based drug design targeting the **JAK3** tyrosine kinase was used to identify a lead quinazoline derivative, **WHI-P131**. Three-dimensional coordinates were constructed for protein tyrosine kinases **JAK1**, **JAK2**, **JAK3**, SYK, and BTK. An anal. of the catalytic site of **JAK3** revealed six nonconserved residues which can interact more favorably with **WHI-P131** and enhance binding relative to other tyrosine kinases. In vitro kinase assays showed that **WHI-P131** inhibited **JAK3** (IC50 .apprx. 10μM) but did not show inhibition of **JAK1**, **JAK2**, SYK, BTK, LYN, or IRK, as predicted by mol. modeling studies. These results may contribute to the identification of new anti-leukemic agents.

=> => d bib abs hitstr tot

L59 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:697825 HCAPLUS
DN 138:248181
TI Treatment of post-bone marrow transplant acute graft-versus-host disease with a rationally designed JAK3 inhibitor
AU Cetkovic-Cvrlje, Marina; Roers, Bertram A.; Schonhoff, Dawn; Waurzyniak, Barbara; Liu, Xing-Ping; **Uckun, Fatih M.**
CS Experimental BMT Program, Parker Hugher Cancer Center, St. Paul, MN, 55113, USA
SO Leukemia & Lymphoma (2002), 43(7), 1447-1453
CODEN: LELYEA; ISSN: 1042-8194
PB Taylor & Francis Ltd.
DT Journal
LA English
AB Here we show that the Janus kinase 3 (JAK3) inhibitor 4-(3'-hydroxyphenyl)-amino-6,7-dimethoxyquinazoline (JANEX-3) exhibits potent anti-GVHD activity and consequently improves the post-BMT survival outcome of C57BL/6 (H-2b) recipient mice transplanted with allogeneic bone marrow/splenocyte (BM/S) grafts from MHC disparate BALB/c mice (H-2d). One hundred percent of the vehicle-treated allograft recipients developed severe GVHD and died with a median survival of 41 days. Treatment of recipient mice with JANEX-3 (30 mg/kg/day, 3 +/day) after the onset of rapidly progressive severe GVHD in the 3rd week after BMT significantly improved the survival of BMT recipients with GVHD and prolonged the median survival time to 78 days ($P < 0.0001$, log-rank test). The probability of survival at two and three months post-BMT was 6±6% and 0±0% for vehicle-treated control mice and 100±0% and 38±17% for mice treated with JANEX-3. These results prompted the hypothesis that JAK3 plays a pivotal role in the pathophysiol. of GVHD. To test this hypothesis, we examined if mice transplanted with allogeneic BM/S grafts from Jak3 knockout mice Jak3-/- develop GVHD. The allografts from (Jak3-/-) C57BL/6 (H-2b) mice rescued MHC-disparate recipient BALB/c mice (H-2d) of the lethal toxicity of TBI without causing fatal GVHD. Taken together, these observations establish JAK3 as a key mediator of severe GVHD after allogeneic BMT in the context of a major-HLA disparity.
IT **211555-08-7**, Janex 3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of post-bone marrow transplant acute graft-vs.-host disease with a rationally designed JAK3 inhibitor)
RN 211555-08-7 HCAPLUS
CN Phenol, 3-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L59 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:63563 HCAPLUS
DN 130:261387
TI Pharmacokinetics and biologic activity of the novel mast cell inhibitor,

4-(3'-hydroxyphenyl)-amino-6,7-dimethoxyquinazoline in mice

AU Chen, Chun-Lin; Malaviya, Ravi; Navara, Christopher; Chen, Hao; Bechard, Brian; Mitcheltree, Greg; Liu, Xing-Ping; **Uckun, Fatih M.**

CS Department of Pharmaceutical Sciences, **Hughes Institute**, St. Paul, MN, 55113, USA

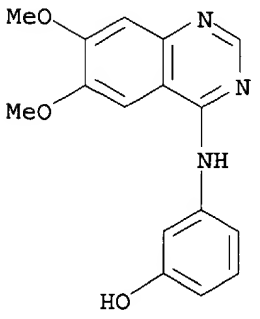
SO Pharmaceutical Research (1999), 16(1), 117-122
CODEN: PHREEB; ISSN: 0724-8741
PB Plenum Publishing Corp.
DT Journal
LA English

AB The purpose of the present study was to examine the pharmacodynamic and pharmacokinetic features of the novel mast cell inhibitor 4-(3'-Hydroxyphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P180) in mice. A high performance liquid chromatog. (HPLC)-based quant. detection method was used to measure plasma WHI-P-180 levels in mice. The plasma concentration-time data was fit to a single compartment pharmacokinetic model by using the WinNonlin program to calculate the pharmacokinetic parameters. A cutaneous anaphylaxis model was used to examine the pharmacodynamic effects of WHI-P180 on anaphylaxis-associated vascular hyperpermeability. The elimination half-life of WHI-P180 in CD-1 mice (BALB/c mice) following i.v., i.p., or p.o. administration was less than 10 min. Systemic clearance of WHI-P180 was 6742 mL/h/kg in CD-1 mice and 8188 mL/h/kg in BALB/c mice. Notably, WHI-P180, when administered in two consecutive nontoxic i.p. bolus doses of 25 mg/kg, inhibited IgE/antigen-induced vascular hyperpermeability in a well-characterized murine model of passive cutaneous anaphylaxis. WHI-P180 is an active inhibitor of IgE-mediated mast cell responses in vitro and in vivo. Further preclin. characterization of WHI-P180 may improve the efficacy of WHI-P180 in vivo and provide the basis for design of effective treatment and prevention programs for mast cell- mediated allergic reactions.

IT **211555-08-7**, WHI-P 180
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(mastocyte inhibitor quinazoline derivative WHI-P180 pharmacokinetics and pharmacodynamics)

RN 211555-08-7 HCAPLUS

CN Phenol, 3-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'HCAPLUS' ENTERED AT 12:39:03 ON 08 MAY 2004

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L2          459 S E4-E11
                E HUGHES/AP,CS
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L3        20026 S E3,E4
                E HUGHES INS/PA,CS
L4           37 S E5-E16
L5         8669 S (HUGHES(L)INSTITUTE?)/PA,CS
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L7            2 S L6 AND 3/NR
                SEL RN
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L10          11 S L9 NOT (COMPD OR WITH)
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L12           3 S L8 NOT L9

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L15          41 S WHI()(P154 OR P131 OR P()(154 OR 131))
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L17           3 S 4 3 BROMO 4 HYDROXYPHENYL AMINO 6 7 DIMETHOXYQUINAZOLINE
L18           5 S 4 3 BROMO 4 HYDROXYLPHENYL AMINO 6 7 DIMETHOXYQUINAZOLINE
L19           3 S 4 4 HYDROXYLPHENYL AMINO 6 7 DIMETHOXYQUINAZOLINE
L20          58 S L13-L19
L21          39 S L2 AND L20
L22          39 S L3-L5 AND L20
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L25          50 S L24
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L29        2935 S L27 CSS FUL SUB=L26
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L47          2230 S L44,L45,L46
L48           323 S (JAK3 OR JAK 3)()(JANUS KINASE OR KINASE OR PROTEIN KINASE OR
L49           709 S JANUS KINASE 3 OR JAK KINASE OR PROTEIN KINASE JAK3 OR LEUKOC
L50             5 S L42 AND L47-L49
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L52             3 S L42 AND JAK 3
L53            10 S L51,L52
L54             3 S L42 AND (CJUN OR C JUN)
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L56            31 S L23 NOT L55
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